University of Padua

School of Medicine

Single-Cycle Master's Degree Course in Medicine and Surgery

Department of Women and Children's Health

Director: Prof. Giorgio Perilongo

Complex Operating Unit of Pediatric and Functional Neurosurgery

Director: Prof. Luca Denaro

THESIS

Surgical Management of Refractory Intracranial Hypertension in Children: Single-Centre Experience Compared to Current Evidence

Supervisor Prof. Luca Denaro

Co-supervisor Dott. Alberto D'Amico

Graduand Bianca Bertirossi

Student Number 1239681

Academic Year 2024/2025

University of Padua

School of Medicine

Single-Cycle Master's Degree Course in Medicine and Surgery

Department of Women and Children's Health

Director: Prof. Giorgio Perilongo

Complex Operating Unit of Pediatric and Functional Neurosurgery

Director: Prof. Luca Denaro

THESIS

Surgical Management of Refractory Intracranial Hypertension in Children: Single-Centre Experience Compared to Current Evidence

Supervisor Prof. Luca Denaro

Co-supervisor Dott. Alberto D'Amico

Graduand Bianca Bertirossi

Student Number 1239681

Academic Year 2024/2025

TABLE OF CONTENTS

ABSTRACT **1**

1 INTRODUCTION **3**

1.1 Brain Injury: Traumatic 3

1.1.1 Definition and epidemiology 3

1.1.2 Classification 4

1.2 Brain Injury: Non-Traumatic 8

1.2.1 Causes and Incidence 8

1.3 Pediatric vs Adult Brain Injury: Anatomical and Physiological Differences 10

1.4 Intracranial Hypertension and raised Intracranial Pressure 12

1.4.1 Pathophysiology and clinical manifestations 12

1.4.2 Initial Assessment and Neuroimaging 17

1.4.3 ICP Monitoring: Invasive and Non-invasive Methods 19

1.4.4 Management of raised ICP in Pediatric Patients 22

1.5 Decompressive Craniectomy 27

1.5.1 Historical Background and Theoretical Rationale 27

1.5.2 Evidence from Clinical Trials: DECRA and RESCUEicp 29

1.5.3 Indications and Current Recommendations 31

1.5.4 Description of the technique 32

1.5.5 Controversies and Ethical Considerations in Pediatric DC 34

1.5.6 Complications 35

1.5.7 Outcomes 37

2 AIM OF THE STUDY **41**

3 MATERIALS AND METHODS **42**

3.1 Study Design and Inclusion Criteria 42

3.2 Systemic Review of the Literature 44

3.3 Statistical Analysis 45
3.3.1 Descriptive Statistics 46
3.3.2 Comparative Analysis 46
3.3.3 Data Cleaning and Handling of Missing Values 47
3.3.4 Rationale for Variable Selection 47
4 RESULTS 48
4.1 Institutional Case Series 48
4.1.1 Demographics and Baseline Characteristics 48
4.1.2 Case reports 51
4.1.3 Outcome Scores 58
4.1.4 Comparative analysis within our Case Series 61
4.2 Literature Cohort 66
4.3 Comparative analysis of long-term Outcomes 74
5 DISCUSSION 77
5.1 Interpretation of Results 77
5.2 Comparison with Literature 81
5.2.1 Age and Etiology 81
5.2.2 Initial Neurological Status and Radiology 81
5.2.3 Timing and Type of Decompressive Craniectomy 82
5.2.4 Postoperative Complications 82
5.2.5 Functional Outcomes (GOSE-Peds) 82
5.2.6 Cranioplasty Timing and Protocols 83
5.3 Cumulative GOSE-Based Outcome Comparison 84
5.3.1 Mortality Rates (GOSE 1) 84
5.3.2 Unfavorable vs Favorable Outcomes (GOSE ≤ 4 vs ≥ 5) 84
5.3.3 Higher Recovery Tiers (GOSE ≥ 7 and GOSE = 8) 84
5.3.4 Methodological Considerations 85
5.3.5 Clinical Implications 85

5.4 General Considerations and Implications 86

5.5 Suggestions for Future Research..... 88

6 CONCLUSIONS 90

7 BIBLIOGRAPHY 91

ABSTRACT

Background

Traumatic brain injury (TBI) is a major cause of morbidity and mortality in the pediatric population worldwide, with long-term consequences affecting neurological, cognitive, and psychosocial development.

Moreover, the pediatric brain exhibits unique anatomical and physiological characteristics that influence both the injury pattern and the response to therapy. Thus, these pathophysiological differences require tailored management strategies focused on maintaining optimal intracranial pressure (ICP) and cerebral perfusion pressure (CPP) to limit secondary brain injury.

When elevated ICP becomes refractory to medical treatment, decompressive craniectomy (DC) may be considered as a second-tier intervention. While its efficacy is supported by adult trials, pediatric evidence remains still very limited. The impact of DC on long-term neurological outcomes in children remains a topic of active investigation, necessitating further research to clarify indications, timing, and expected benefits in this patient population.

Aim of the Study

This study aims to describe and analyze the experience of the University Hospital of Padua in the management of pediatric patients undergoing decompressive craniectomy. The objective is to compare local clinical outcomes with those reported in the international literature, to highlight similarities, discrepancies, and potential areas for improvement in the therapeutic approach.

Materials and Methods

A retrospective observational study was conducted at the University Hospital of Padova, analyzing medical records of pediatric patients who underwent decompressive craniectomy between January 2012 and December 2024. Inclusion criteria comprised all patients under 16 years of age who received a primary or secondary DC, regardless of the underlying etiology.

Clinical and radiological data were extracted from patient electronic charts, together with neuroimaging findings, both pre- and post-operative, as well as clinical outcomes until the last available follow up.

Data analysis was made using Microsoft Excel and RStudio and results were compared with findings from the existing literature on pediatric DC, particularly focusing on retrospective cohort studies.

Results

Data analysis is currently ongoing. A total of 11 patients, aged between 0 and 13 ± 4 years, were included in the study. Preliminary findings suggest that the clinical characteristics and outcomes observed in the Padua cohort are consistent with those reported in published studies. Early results indicate an association between factors, such as age, GCS at admission, pupillary symmetry and midline shift, and clinical outcome, assessed using the Pediatric Extended Glasgow Outcome Scale (GOSE-Peds).

Conclusions

Although data are still being processed, preliminary results appear to align with existing evidence in the literature. Further analysis is expected to provide a more comprehensive understanding of outcome predictors.

1 INTRODUCTION

1.1 Brain Injury: Traumatic

1.1.1 Definition and epidemiology

Traumatic brain injury (TBI) is defined as an alteration in brain function, or other evidence of brain pathology, caused by an external mechanical force[1] such as a blow, jolt, or penetrating injury to the head. In pediatric patients—including children over one year of age, adolescents, and young adults—TBI remains a leading cause of morbidity and mortality globally, often resulting in long-term consequences that affect physical, cognitive, and emotional development.

The incidence, severity, and etiology of pediatric TBI vary considerably across countries and age groups, influenced by socioeconomic status, healthcare infrastructure, and the effectiveness of prevention strategies. Globally, the incidence of pediatric TBI is estimated to range between 47 and 280 cases per 100,000 children annually, with higher rates in low- and middle-income countries due to poor enforcement of safety regulations, limited access to specialized trauma care, and a general lack of public awareness.[2] In high-income nations, TBI accounts for approximately 30–50% of all pediatric trauma-related hospital admissions, with most cases classified as mild (Glasgow Coma Scale 13–15).[3]

Age-specific patterns reveal peak incidence in toddlers (ages 0–4) and adolescents (ages 15–19).[2] The leading causes of injury differ by age: falls are predominant among younger children, whereas road traffic accidents (RTAs), sports injuries, and interpersonal violence become more relevant during adolescence. RTAs in particular, are a leading cause of TBI-related death in the pediatric population worldwide, especially in regions lacking stringent road safety enforcement.[4]

In Italy, comprehensive national data on pediatric TBI remain limited; however, existing studies and hospital records suggest an incidence of approximately 200 cases per 100,000 children per year—comparable to rates observed in other Western European countries.[5] According to a European-wide pediatric injury survey, falls are the predominant mechanism of injury in children under 10, while motor vehicle collisions and bicycle-related incidents become more frequent in

older children and adolescents, reflecting an age-dependent shift in trauma patterns.[6] Although a substantial proportion of pediatric TBIs in Italy are classified as mild, severe cases—though less common—constitute a significant portion of admissions to pediatric neurocritical care units, particularly in major trauma centers such as those in Milan, Rome, and Padua.

The burden of pediatric TBI extends beyond acute mortality and morbidity. Children with moderate to severe injuries are at heightened risk of chronic neurological, cognitive, and psychosocial sequelae, which often translate into long-term disability and substantial socioeconomic costs. These challenges are especially significant in healthcare systems with limited pediatric neurorehabilitation services.[7] In recent years, Italy has made progress in enhancing pediatric trauma care through the development of regional trauma systems and the implementation of national guidelines. Several regions, such as Lombardy, Tuscany, and Lazio, have established structured pediatric trauma networks with designated referral centers and standardized care pathways. In the Veneto region, pediatric trauma management relies on the integration of specialized services, including our Pediatric Neurosurgery Unit at the University Hospital of Padua, which serves as a regional referral center for complex traumatic brain injuries. Post-acute care and neurorehabilitation are supported by institutes such as the IRCCS E. Medea centers in Conegliano and Pieve di Soligo, while the Neonatal Emergency Transport System (NETS) ensures coordinated inter-hospital transfers of critically ill pediatric patients.

1.1.2 Classification

Head injuries in pediatric patients encompass a wide range of extracranial and intracranial lesions, often classified anatomically and temporally. Scalp lacerations, though external, may be a source of significant blood loss and can obscure underlying skull fractures or CSF leaks. They may present with deceptively minor bleeding on arrival, only to bleed more profusely after resuscitation and blood pressure normalization.[8]

Cranial vault fractures can be linear—typically benign and self-limiting—or depressed, which may require surgical intervention if associated with CSF leakage, parenchymal damage, or depression >1 cm. Fractures overlying dural venous

sinuses carry risks of air embolism and hemorrhage. Basal skull fractures may manifest with raccoon eyes, Battle's sign, CSF rhinorrhea/otorrhea, or cranial nerve palsies. Temporal bone fractures can be detected via otoscopic evaluation and may involve VII or VIII cranial nerves. Clival fractures necessitate high suspicion for vascular injury and cranial neuropathies, while occipital condyle fractures, although rare (0.4–0.7% in major trauma), may indicate craniocervical instability and require MRI assessment.[9]

Pneumocephalus results from air entry into the cranial cavity and, when tension develops, can exert mass effect and lead to rapid neurologic deterioration.[9]

Regarding the intracranial lesions, they can occur in isolation or combination and are influenced by both the mechanism of injury and the developmental characteristics of the skull and brain.

Epidural hematoma (EDH) arises from bleeding between the inner table of the skull and the dura mater, usually due to laceration of the middle meningeal artery or dural venous sinuses. They are often associated with linear skull fractures, particularly in the temporoparietal region. In children, because the dura is more tightly adherent to the skull, EDHs are less common than in adults but can still occur with high-energy trauma. Clinically, EDH may present with the classic "lucid interval": an initial brief loss of consciousness, followed by apparent recovery and subsequent neurological deterioration. Symptoms include vomiting, headache, seizures, hemiparesis, and eventually signs of herniation such as anisocoria and coma. Early diagnosis and urgent surgical evacuation are often lifesaving.[10][8]

Subdural hematoma (SDH) results from rupture of bridging veins between the cerebral cortex and dural sinuses, leading to blood accumulation in the subdural space. SDHs are more frequent in pediatric patients, particularly in infants and young children, due to the increased mobility of the brain within the skull and immature myelination. Mechanisms include acceleration-deceleration injuries, birth trauma, and in some cases, non-accidental trauma (NAT). Clinically, SDH may cause altered consciousness, seizures, irritability, and bulging fontanelles in infants. Unlike EDH, symptoms often evolve more gradually, although acute SDH

can lead to rapid deterioration. Chronic SDH, especially in infants, may be asymptomatic or cause subtle developmental regression.[11]

Subarachnoid hemorrhage (SAH) involves bleeding into the subarachnoid space, often from tearing of small pial vessels overlying the brain surface. It can occur as an isolated lesion or in combination with other hemorrhages, especially in high-velocity injuries. SAH in children may present with headache, photophobia, nuchal rigidity, and vomiting. In more severe cases, altered mental status or seizures may occur. CT imaging shows blood within the cisterns and sulci. Traumatic SAH carries a risk of vasospasm and hydrocephalus, though these are more commonly studied in the context of aneurysmal SAH in adults.[9]

Intracerebral hemorrhage (ICH), also known as intraparenchymal hematoma, occurs within the brain parenchyma itself and is typically the result of direct contusional injury, shear forces, or extension of subarachnoid or subdural bleeding. In children, traumatic ICHs are most commonly located in the frontal and temporal lobes. Clinical presentation depends on the size and location of the bleed, and may include focal neurological deficits, reduced consciousness, or seizures. ICHs can increase intracranial pressure significantly and may require surgical decompression if mass effect or herniation risk develops.[12]

Intraventricular hemorrhage (IVH) is less common in older children but may be seen in neonates and infants following severe TBI or in association with parenchymal contusions and SAH. Blood in the ventricular system may obstruct CSF flow, leading to acute hydrocephalus. Signs include rapid head circumference increase in infants, vomiting, bradycardia, and altered consciousness. IVH may require external ventricular drainage and long-term CSF diversion.[10]

Diffuse axonal injury (DAI) stems from rotational acceleration-deceleration forces leading to shearing at gray-white matter interfaces. The Adams classification defines three grades: Grade I: Axonal injury in cortex, subcortical white matter; Grade II: Focal lesions in corpus callosum; Grade III: Additional lesions in brainstem. Clinical manifestations range from mild post-concussive symptoms to persistent vegetative state with central autonomic dysfunction (e.g., hyperthermia,

tachypnea, posturing). MRI is the gold standard for diagnosis, as CT often appears normal.[13]

Other types of injuries are penetrating head injuries—whether missile or non-missile—resulting in extensive parenchymal disruption. Primary injury is compounded by secondary cerebral edema, elevated ICP, and decreased CPP. These injuries also carry a high risk of delayed complications including abscess, traumatic aneurysms, AVFs, seizures, and migration-related hematomas.[11]

Lastly, abusive head trauma (AHT) represents a distinct and severe form of pediatric traumatic brain injury, typically occurring in infants under the age of two and often resulting from violent shaking, blunt impact, or a combination of both. Clinically, AHT frequently presents with a triad of findings: subdural hemorrhage, retinal hemorrhages, and encephalopathy, although this triad is neither necessary nor sufficient for diagnosis. Compared to accidental trauma, AHT is more commonly associated with bilateral or multiple subdural hematomas, interhemispheric bleeding, diffuse axonal injury, and brain swelling, often without external signs of trauma. Additional findings may include cervical spinal cord injury, especially in the craniocervical junction, which is increasingly recognized via MRI as a potential marker of AHT. Due to its often occult presentation and high risk of recurrence or fatality, AHT requires a multidisciplinary diagnostic approach integrating neuroimaging, ophthalmological findings, clinical history, and social evaluation. Early recognition is crucial to safeguard the child and prevent further harm.[14]

1.2 Brain Injury: Non-Traumatic

1.2.1 Causes and Incidence

Non-traumatic brain injuries (NTBIs) refer to structural or functional damage to the brain that is not caused by external mechanical force. In pediatric populations, these injuries represent a heterogeneous group of conditions that, while less common than traumatic brain injuries, are associated with significant morbidity and mortality. NTBIs are an important but often under-recognized cause of acute neurological deterioration in children, accounting for up to 25–30% of all pediatric intensive care unit (PICU) admissions for acute brain injury.[15] Epidemiological data on NTBI in children are limited and vary widely depending on the condition and geographic region. However, population-based studies suggest that NTBIs may occur at an estimated rate of 10 to 30 per 100,000 children annually, with the highest incidence seen in neonates and infants due to the increased vulnerability of the developing brain.[16,17] These conditions are often life-threatening and require urgent neurocritical care, yet they remain less studied and less standardized in management compared to TBIs.

The etiologies of NTBI are diverse, including spontaneous intracerebral hemorrhage, arterial ischemic stroke, cerebral venous sinus thrombosis, hypoxic-ischemic encephalopathy, central nervous system infections, and metabolic or genetic encephalopathies. The clinical presentation is variable and may range from subtle changes in mental status to rapid neurological decline.

Among the most prevalent and clinically significant causes of NTBI in children are the following:

- Spontaneous Intracerebral Hemorrhage (ICH): ICH in children is most often associated with underlying vascular anomalies, such as arteriovenous malformations (AVMs), cavernous angiomas, and aneurysms. Additional causes include coagulopathies, tumors, and idiopathic cases. The estimated incidence is 1–2 per 100,000 children annually, with neonates at particular risk.[18]
- Arterial Ischemic Stroke (AIS): Pediatric AIS is a multifactorial condition with risk factors including congenital heart disease, infections, arteriopathies (e.g., moyamoya disease), and prothrombotic disorders. The

incidence ranges from 1 to 8 per 100,000 children per year. Early diagnosis is often delayed, impacting prognosis.[19]

- Cerebral Venous Sinus Thrombosis (CVST): CVST is a rare but serious NTBI subtype involving thrombosis of the cerebral venous system. It accounts for approximately 0.6–0.7 per 100,000 pediatric cases annually, most commonly in neonates. Risk factors include dehydration, systemic infection, and inherited thrombophilias.[20]
- Hypoxic-Ischemic Encephalopathy (HIE): Although classically associated with the neonatal period, HIE may occur in older children in contexts such as drowning, cardiac arrest, or severe systemic hypotension. It is a leading cause of neurological disability and death in newborns, with incidence in term infants ranging from 1 to 6 per 1,000 live births.[21]

In contrast to TBIs, NTBIs often lack the dramatic precipitating event that prompts immediate medical evaluation, resulting in delayed recognition and treatment. Furthermore, the lack of high-quality pediatric data and standardized guidelines limits the development of evidence-based protocols. Greater awareness and continued research into the epidemiology and pathophysiology of NTBI are essential to improve outcomes and guide resource allocation in pediatric neurocritical care.

1.3 Pediatric vs Adult Brain Injury: Anatomical and Physiological Differences

Traumatic brain injuries are particularly concerning in the pediatric population due to the unique anatomical and physiological characteristics of the developing brain.[22] These differences not only affect the mechanisms of injury but also the brain's response to trauma and its capacity for recovery.

Anatomically, the pediatric brain differs significantly from the adult brain in terms of skull morphology and biomechanical properties. Children have smaller and more compliant skulls, with open sutures and fontanelles that allow limited expansion in response to increased intracranial pressure. However, this flexibility also makes the skull less capable of withstanding external forces. Moreover, children's heads are proportionally larger and heavier relative to their body size, and their neck musculature is underdeveloped, increasing susceptibility to acceleration-deceleration injuries such as whiplash. While the softness and plasticity of the pediatric skull may provide some mechanical buffering, they also predispose to diffuse axonal shear injuries, resulting in global brain swelling and intracranial hypertension, rather than the focal mass lesions typically seen in adult patients.[23]

Physiologically, the pediatric brain exhibits several features that influence both the primary and secondary phases of injury. Cerebral autoregulation is thought to be immature in children, particularly after severe trauma, potentially resulting in vasodilation and diffuse cerebral hyperemia. Moreover, the pediatric cerebral vasculature is less developed than that of adults, which may contribute to an exaggerated response to systemic and intracranial insults.[22] Cerebral blood flow (CBF) is age-dependent and generally higher in children than in adults. It peaks between the ages of 3 and 8 years, with reported values reaching up to 100 mL/100 g/min, nearly twice the adult average of 50 mL/100 g/min. This elevated perfusion correlates with periods of intense synaptic activity and neuronal growth but also increases the risk of hyperemia and secondary injury following TBI.

Cerebral blood volume (CBV) is similarly increased in pediatric patients due to greater vascular density and perfusion requirements. While this supports neurodevelopment, it reduces intracranial compliance, such that even small increases in volume—due to edema or hemorrhage—may precipitate a significant rise in intracranial pressure.[24]

The cerebral metabolic rate for oxygen ($CMRO_2$) and glucose (CMRglc) are also markedly higher in children. During early childhood, the brain may account for up to 50% of the body's total glucose utilization, compared to approximately 20% in adults.[25] This intense metabolic demand makes the pediatric brain especially vulnerable to hypoxia and ischemia, which are common contributors to secondary brain injury.

Understanding these age-related anatomical and physiological characteristics is crucial when managing pediatric TBI. Interventions aimed at maintaining adequate cerebral perfusion and controlling intracranial pressure must be adapted to the pediatric context. Strategies that are effective in adult patients may be suboptimal—or even harmful—in children, thus, pediatric-specific research and management protocols are essential to improve outcomes in this population.

1.4 Intracranial Hypertension and raised Intracranial Pressure

1.4.1 Pathophysiology and clinical manifestations

Intracranial hypertension (ICHTN), defined as a sustained elevation of intracranial pressure (ICP), is a life-threatening complication of both traumatic and non-traumatic brain injury. In pediatric patients, elevated ICP is especially critical due to the heightened vulnerability of the developing brain to ischemia and secondary insults. Its management requires a precise understanding of intracranial dynamics, pathophysiological cascades, and clinical implications.

Normal ICP varies with age and body posture but is generally considered to be 5–15 mmHg in healthy supine adults, 3–7 mmHg in children and 1,5–6 mmHg in infants.[26]

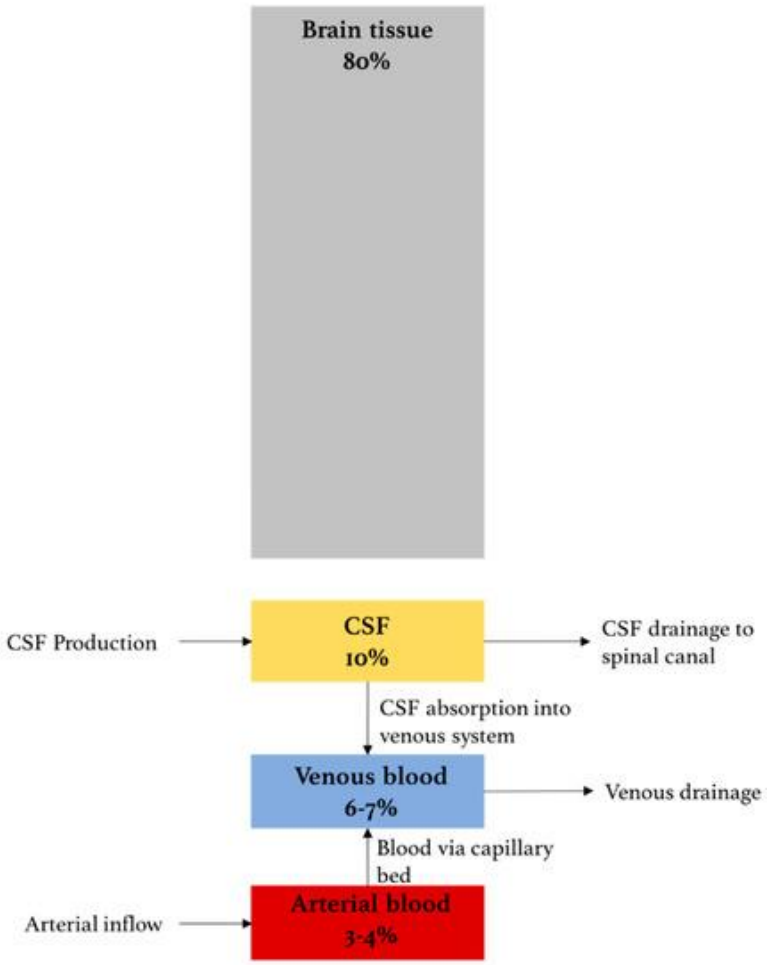


Figure 1 - The Monro-Kellie model[27]

The Monro-Kellie doctrine, first postulated by Alexander Monro and expanded by George Kellie, remains the conceptual basis for understanding ICP regulation.

It states that the cranial vault has a fixed volume consisting of three components: brain parenchyma (~80%), cerebrospinal fluid (CSF, ~10%), and intracranial blood (~10%) (*Fig. 1*).[28] In the average adult male the intracranial volumes approximate to 1,450 ml for the brain, 110 ml blood, and 65 ml of CSF.[29] Because the skull is a rigid compartment, any increase in the volume of one component must be compensated by a reduction in one or both of the others to avoid a rise in ICP. This compensatory mechanism becomes clinically significant when a new intracranial volume is introduced, whether physiological—such as the cyclic arterial blood inflow during systole—or pathological, as in the case of a hematoma, tumor, or cerebral swelling. Initially, this added volume is accommodated through the displacement of CSF into the spinal subarachnoid space and the compression of venous blood volume, maintaining a relatively stable ICP. However, as these compensatory reserves become exhausted—beginning with the CSF, followed by venous blood and ultimately arterial blood—the system enters a decompensatory phase where even small volume increases lead to exponential rises in ICP. This dynamic is visually represented by the Langfitt curve (*Fig.2*), which illustrates the relationship between intracranial volume and ICP over time.

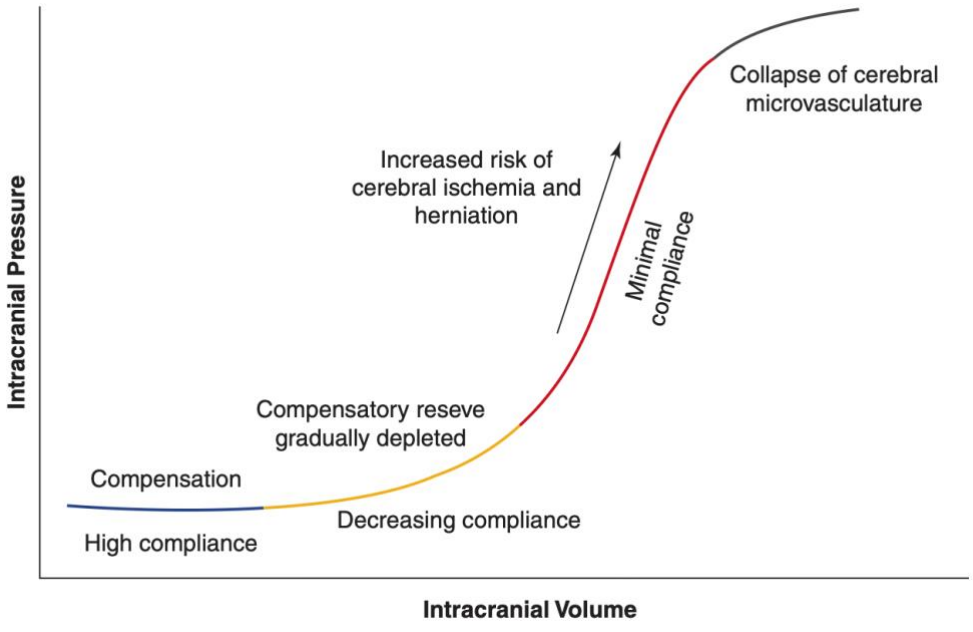


Figure 2 - Langfitt curve[11]

The Langfitt curve is typically divided into four phases. In Phase I, compensatory mechanisms allow for volume expansion through CSF displacement without a significant change in ICP. Phase II begins as the CSF buffering capacity is exhausted, leading to local perfusion changes, metabolic acidosis, and the activation of vasodilatory cascades that increase intracranial blood volume. In Phase III, the loss of cerebral autoregulation contributes to an exponential rise in ICP, which may eventually approach or exceed the mean arterial pressure (MAP), resulting in a critical reduction in cerebral perfusion pressure (CPP). When CPP becomes insufficient to sustain cerebral blood flow, Phase IV starts, being characterized by vasoplegia, neuronal ischemia, and eventual brain death.[30]

Thus, cerebral autoregulation (*Fig. 3*) can be overwhelmed by MAP increases and blood pressure (BP) failure, and even in chronic hypertensive patients, where the MAP thresholds are shifted to the right making the brain more sensible to low blood pressures values. The relationship between MAP and CPP is expressed by the equation $CPP = MAP - ICP$, where the cerebral venous pressure is approximated by the ICP. This concept emphasizes that the primary mechanism of cerebral injury from ICHTN is cerebral ischemia due to compromised cerebral perfusion.

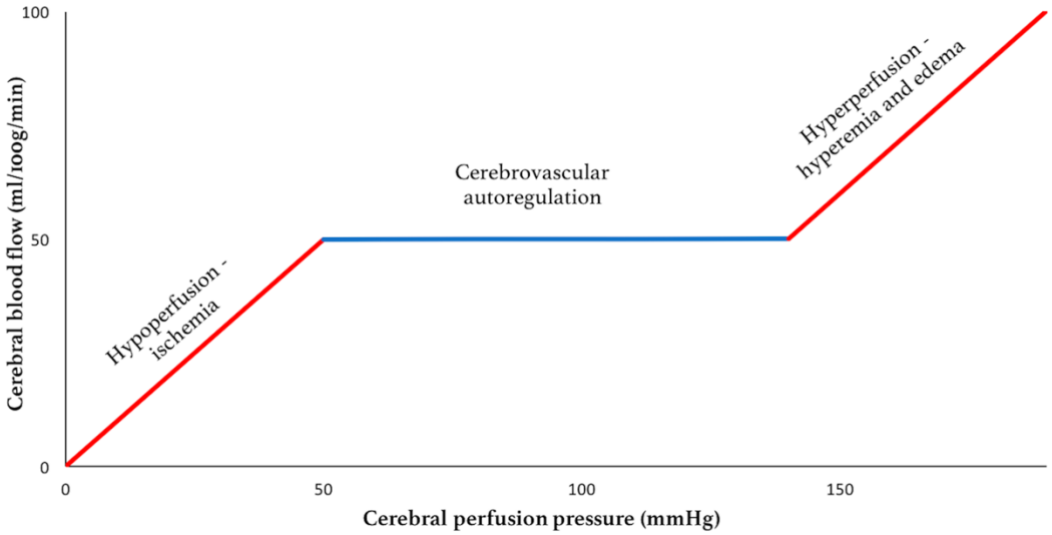


Figure 3 - Cerebral autoregulation capacity(27)

However, beyond this volumetric balance, intracranial hypertension reflects complex secondary injury pathways that go beyond mass effect and compliance limits. Cerebral edema, a principal driver of raised ICP, is defined as an increase in

brain water content.[29] It may be cytotoxic (due to cellular injury, meaning intracellular water accumulation from ionic pump failure) or vasogenic (resulting from the disruption of the blood-brain barrier). In pediatric patients, the immature and more permeable blood-brain barrier increases susceptibility to fluid extravasation and subsequent edema.[31]

Additionally, impaired cerebral autoregulation is frequently observed in children with severe TBI or acute brain injury. When autoregulatory control is lost, cerebral perfusion becomes pressure-passive: hypotension may lead to ischemia, while hypertension may exacerbate hyperemia and edema.

Another contributor to elevated ICP is venous outflow obstruction, leading to venous congestion, increased intracranial blood volume, and in severe cases, hemorrhagic infarctions, especially in vulnerable watershed regions.

The numerous causes of raised ICP (*Table 1*) can occur individually or in various combinations and can be further divided into primary or secondary depending on the pathology. In primary causes of increased ICP, its normalization depends on rapidly addressing the underlying brain disease. In secondary causes of raised ICP the underlying systemic or extracranial disorder has to be managed.[32]

Table 1- Causes of raised ICP[32]

Increased brain volume
Intracranial space occupying lesions
Brain tumors
Brain abscess
Intracranial hematoma
Intracranial vascular malformation
Cerebral edema
Encephalitis (viral, inflammatory)
Meningitis
Hypoxic ischemic encephalopathy
Traumatic brain injury
Hepatic encephalopathy
Reye's syndrome
Stroke
Reye's syndrome
Increase in CSF volume
Hydrocephalous
Choroids plexus palpilloma
Increased blood volume
Vascular malformations
Cerebral venous thrombosis
Meningitis, encephalitis

Although there are various causes of raised ICP, there are some key clinical manifestations, which are often subtle at onset but can rapidly progress.

Acute symptoms of raised ICP usually are headache, decreased level of consciousness, nausea, vomiting, irritability, worsening sensorium and cranial nerve palsies, especially sixth nerve palsy (resulting in diplopia), may indicate early brainstem involvement. Papilledema and other visual disturbances, such as blurred vision, transient visual obscurations, and potentially permanent vision loss, are consequences of chronic raised ICP. Cushing's triad (hypertension, bradycardia, and irregular respirations), although with all its three components is uncommon, signals impending brain herniation and late phases of intracranial hypertension.[11]

1.4.2 Initial Assessment and Neuroimaging

As with any sick patient, the first step is the assessment and management of the airways, breathing and circulatory function. Another priority is looking for potential signs of brain herniation (*Table 2*), because if these are present, immediate measures to decrease ICP should be performed.

Table 2 - Clinical recognition of herniation symptoms[32]

Type of herniation	Clinical manifestations
Subfalcine herniation (medially, of the cingulate gyrus)	Impaired consciousness, *monoparesis of the contralateral lower extremity*[a]
Central transtentorial	Impaired consciousness, abnormal respirations, *symmetrical small reactive*[a] or midposition fixed reactive pupils, *decorticate*[a] evolving to decerebrate posturing
Lateral transtentorial (downward and medially of uncus and parahippocampal gyrus)	Impaired consciousness, abnormal respirations, *third nerve palsy*[a] (unilateral dilated pupil, ptosis), *hemiparesis*[a]
Upward Transtentorial (upward of the cerebellar vermis and midbrain)	Prominent brainstem signs, downward gaze deviation, upgaze palsy, decerebrate posturing
Transforaminal (downward of cerebellar tonsils and medulla)	Impaired consciousness, neck rigidity, opisthotonus, decerebrate rigidity, vomiting, irregular respirations, apnea, bradycardia

[a] Clinical signs of potentially reversible brain herniation

Glasgow Coma Scale (GCS) is also used as initial assessment of these patients, particularly those with head injuries. This numerical scale (*Table 3*) consists in three components, collectively assessing the patient's responsiveness: eye opening, verbal response and motor response. The seriousness of brain injury is classified accordingly: mild (13 to 15 points), moderate (9 to 12), or severe (3 to 8). Patients with a rating of less than 8 are by definition in coma.[33]

Although the Glasgow Coma Scale remains the cornerstone of initial neurological assessment in patients with acute brain injury, its applicability in the pediatric population—particularly in infants and young children—has long been debated due to limitations in assessing verbal and motor responses across developmental stages. For this reason, pediatric-specific adaptations of the scale, such as the Pediatric Glasgow Coma Scale (GCS-Peds), have been proposed and validated to provide a more developmentally appropriate assessment of consciousness. The GCS-Peds modifies response categories to reflect age-appropriate behaviors and has demonstrated improved reliability and prognostic accuracy in preverbal and non-cooperative children. While its use is not yet fully standardized across centers, growing evidence supports its integration into emergency and intensive care settings for more precise stratification of injury severity in pediatric patients.[34]

Table 3 – Comparison between standard GCS and Pediatric GCS[35]

	Score	Standard GCS	Pediatric GCS
Eye opening	4	Spontaneous	Spontaneous
	3	To voice	To voice
	2	To pain	To pain
	1	None	None
Verbal response	5	Oriented	Coos/babbles
	4	Confused	Irritable/cries
	3	Inappropriate words	Cries to pain
	2	Incomprehensible sounds	Moans
	1	None	None
Motor response	6	Follows commands	Spontaneous movement
	5	Localizes pain	Withdraws to touch
	4	Withdraws to pain	Withdraws to pain
	3	Abnormal flexure posturing	Abnormal flexure posturing
	2	Abnormal extension posturing	Abnormal extension posturing
	1	None	None

Physical examination has low sensitivity to diagnose intracranial hypertension, however findings on the general examination may provide clues to the underlying cause for raised ICP (e.g. jaundice/hepatomegaly in hepatic encephalopathy, rash in viral encephalitis etc.). A recent meta-analysis(36) explored the utility of 3 common physical examination findings for raised ICP: any pupillary dilation, motor posturing and GCS ≤ 8. Although no single finding was diagnostic of the condition, pupillary dilation was found to be highly specific (85.9%) but not sensitive (28.2%). In contrast, a Glasgow Coma Scale of 8 or below was quite sensitive (75.8%) but poorly specific (39.9%). In extremis or if left untreated, patients may develop brain death, meaning the complete and irreversible loss of all brain function. Thus, prompt intervention in elevated ICP, is key and should not be delayed by further investigations.

In the emergency room the imaging study of choice is computed tomography (CT). CT scan allows to find evidence of compression or obliteration of mesencephalic cisterns, midline shift, or one or more lesions. In a non-emergency context, adding to this neuroimaging study contrast media is helpful in distinguishing features of infections and tumors, as well as in the assessment of physiologic process: the blood perfusion and for the depiction of the vessel compartment (angiography/venography).

If the CT scan does not show any abnormalities but the suspicion of raised ICP is still very likely, then an MRI (Magnetic Resonance Imaging) with venogram must be obtained once the patient is stabilized. MRI can detect early stroke, venous

thromboses, posterior fossa tumors and demyelinating lesions which might be missed on CT.[32]

1.4.3 ICP Monitoring: Invasive and Non-invasive Methods

The ICP tracing at monitoring is a ballistic waveform similar to the systemic arterial pressure curve (*Fig. 4*). It is characterized by a narrow "pulse pressure" and is expressed as its mean measured in millimeter of mercury (mmHg). The normal mean ICP is generally between 5-10 mmHg, and it fluctuates to higher levels depending on physiological factors such as body position. The ICP wave contains three consecutive peaks in descending order, Peak 1 to 3 which are called respectively percussion wave, tidal wave, and dicrotic wave.[29]

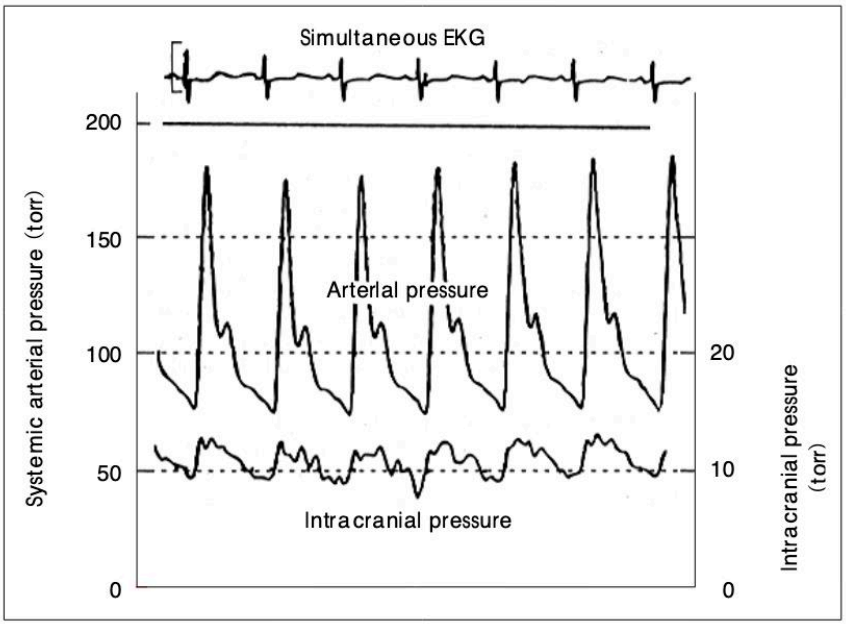


Figure 4 - ICP tracing compared to systemic arterial pressure[29]

Invasive intracranial monitoring remains the gold standard for measuring and diagnosing elevated ICP. According to the 2019 Brain Trauma Foundation (BTF) Guidelines[37], ICP monitoring is recommended in pediatric patients with a Glasgow Coma Scale (GCS) ≤ 8 and abnormal neuroimaging, such as cerebral edema, midline shift, or compressed ventricles. It may also be considered in children with normal imaging but clinical signs of raised ICP, including unexplained unconsciousness, posturing, or pupil asymmetry, as well as in patients at high risk

due to conditions like hydrocephalus, cerebral venous sinus thrombosis, or malignant ischemic stroke.

Invasive ICP monitoring remains the gold standard, particularly through the insertion of an intraventricular catheter, which is the most accurate method but also the only one allowing both monitoring and therapeutic drainage of cerebrospinal fluid.[38] This technique is commonly performed via Kocher's point, located 11 cm posterior to the glabella and 2–3 cm lateral to the midline, avoiding critical neurovascular structures such as the superior sagittal sinus and motor cortex. After standard asepsis and burr-hole creation, the catheter is introduced no more than 7 cm toward the foramen of Monro, allowing for CSF outflow and pressure transmission.[26] In particular, external ventricular drainage (EVD) is the most used one, allowing both ICP monitoring and the possibility to perform, either continuous or intermittent, CSF drainage.[38]

However, ventricular catheters are less feasible in the presence of midline shift or obliterated ventricles and carry risks such as infection and hemorrhage. For this reason, many pediatric centers use intraparenchymal monitors, which are easier to insert and less invasive, though they do not allow for CSF drainage. Less frequently used modalities include subdural and subarachnoid devices, which offer limited accuracy and are largely obsolete in current practice.[29] *Table 4* summarizes the advantages and disadvantages of ICP monitoring based on catheter placement.

Table 4 – ICP monitoring locations[39]

Location	Advantages	Disadvantages
Intraventricular	"Gold standard" Reliability CSF drainage Waveform	Increased risk of infection Potential for brain injury Placement Fluid-filled system Transducer repositioning
Intraparenchymal	Ease of placement Non fluid-filled	Potential for brain injury Increased risk of infection No CSF drainage Catheter breakage
Subarachnoid	Ease of placement No brain penetration Less risk of infection	Questionable accuracy No CSF drainage Fluid-filled system Brain tissue obstruction
Epidural	Dura remains intact Non fluid-filled Ease of insertion	Questionable accuracy No CSF drainage "Wedge effect"

Two major device types are used:

- Fluid-filled systems: connect the catheter to an external transducer (typically aligned with the tragus, approximating the foramen of Monro). Although these allow CSF drainage and administration of agents like fibrinolytics or antibiotics, they also carry a higher infection risk due to the open system.(40)
- Transducer-tipped catheters: include fiberoptic or strain gauge microchip sensors embedded at the catheter tip, allowing direct in situ pressure measurement. These are less prone to calibration drift and more suitable for long-term monitoring.(41)

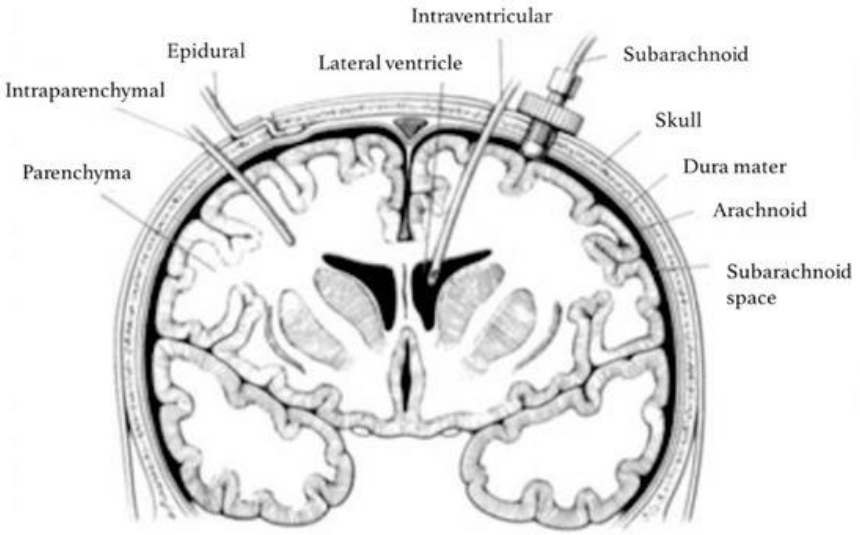


Figure 5 - Sites for Invasive ICP Monitoring(39)

Non-invasive approaches have gained attention, particularly in settings where invasive techniques are contraindicated or unavailable, though none can yet replace direct ICP measurement. Among these, optic nerve sheath diameter (ONSD) ultrasound offers indirect evidence of raised ICP through the distension of the subarachnoid space. This method is based on the fact that when the optic nerve exits the intracranial space entering the orbit, it is still surrounded by the dural sheath, thus the subarachnoid space enveloping the nerve is contiguous with the intracranial one. Any elevation of ICP leads to dilation of the optic nerve sheath, which is detected via transocular ultrasonography. Another method, mainly used in the neurocritical setting, is the transcranial Doppler (TCD) ultrasound. This technique provides an estimate of cerebral hemodynamics by monitoring changes in CBF

velocity. Other methods using Doppler technology include venous transcranial Doppler and ophthalmic artery Doppler, but only few studies have been conducted and both measurements have technical difficulties, preventing their widespread adoption into clinical care.

Near-infrared spectroscopy (NIRS) offers insight into cerebral oxygenation by emitting near-infrared light onto the surface of the head. This technique is limited by its reduced accuracy resulting from scalp and skull injury and possible pathological changes in baseline saturation, thus NIRS is unreliable for widespread use and cannot guide acute intervention.

Fundoscopy is often used as screening method for suspicion of raised ICP, however the technique is operator dependent and, since the process of optic disc swelling takes time, it cannot be applied in emergency situations.

In children with monitored ICP, the BTF[37] recommends treating sustained elevations above 20 mmHg. However, although evidence remains limited, some studies suggest that thresholds should be adapted by age, particularly in neonates or infants with lower baseline ICPs. Despite its central role, ICP monitoring is not without controversy. Invasive procedures pose risks, and the clinical benefit of ICP monitoring appears to be maximized only when it is paired with well-defined, protocol-driven treatment strategies. Thus, pressure values must be interpreted cautiously and integrated with the patient's clinical status and neuroimaging.[26][42]

1.4.4 Management of raised ICP in Pediatric Patients

The management of elevated ICP in children with acute brain injury, aims to prevent or limit secondary brain damage, that is a process that unfolds over hours to days after the initial mechanical insult and is characterized by a complex interplay of inflammation, excitotoxicity, oxidative stress, mitochondrial dysfunction, cerebral edema, and impaired cerebral perfusion.[43]

As cited previously, guidelines from the Brain Trauma Foundation (2019) recommend maintaining ICP below 20 mmHg and CPP between 40–50 mmHg, adjusted for age. This CPP range is suggested to ensure that the minimum value of 40 mm Hg is not breached, moreover there may be age-specific thresholds, with infants at the lower end and adolescents at or above the upper end of this range.

General measures have low risk of adverse effects, thus can be used in all patients with suspected elevated ICP. These include:

- Rapid treatment of hypoxia, hypercarbia, and hypotension as even brief derangements in these parameters can adversely affect outcome. Isotonic fluids, such as normal (0,9%) saline, should be administered to patients to maintain adequate MAP.
- Head-of-bed elevation (30°) to promote venous drainage.
- Avoidance of hypo/hyperthermia, as temperature dysregulation exacerbates neuronal injury.
- Sedation and analgesia, aimed at reducing metabolic demand and preventing agitation-induced ICP surges.[44]

If these strategies fail to maintain ICP within target thresholds or impending signs of herniation are present, second-tier therapies may be considered. These include:

- Hyperosmolar therapy (Level II, III)

  Although evidence is limited regarding the best single drug regimen for osmolar therapy in children with increased ICP, either mannitol or hypertonic saline are used and have similar effects in reducing ICP. For the acute treatment of brain herniation, some experts prefer mannitol.(38) Instead for children with severe TBI (GCS ≤8) suggest hypertonic saline as the first-line agent.
- Controlled hyperventilation (Level III)

  Hyperventilation lowers $PaCO_2$ and causes cerebral vasoconstriction, transiently reducing ICP. This therapeutic intervention carries a high risk of cerebral ischemia, therefore is reserved for episodes of acute brain herniation or ICP elevation that fail to respond to general measures and/or hyperosmolar therapy. Temporary therapeutic hyperventilation ($PaCO_2$ 30 to 35 mmHg) may be initiated under direction by a neurosurgeon for patients with signs of impending herniation in whom surgical intervention is planned. Instead, aggressive hyperventilation ($PaCO_2$ <30 mm Hg) is indicated only if there are clinical signs of acute herniation.
- CSF drainage (Level III)

CSF diversion is often the first treatment of choice for children with refractory intracranial hypertension that is confirmed by an intraparenchymal monitoring device.

- Barbiturates (Level III)

  Barbiturate coma, especially with agents like thiopental, is reserved for refractory ICP as it induces burst suppression on EEG decreasing cerebral metabolic rate, which causes a reduction in CBF and thus ICP. It may also provide a protective effect for the brain tissue during periods of hypoperfusion or hypoxia.[45]

- Analgesics, sedatives, and neuromuscular blockade (Level III)

  Analgesics and sedatives are needed for comfort and tolerance in the management of pediatric severe TBI requiring tracheal intubation and mechanical ventilation. Neuromuscular blocking agents, instead, are not routinely required, except in case of rapid sequence intubation (RSI). Muscle relaxation can also prevent shivering, fighting against the mechanical ventilator, and allows hyperventilation if required.

- Decompressive craniectomy (Level IIA – to improve mortality and overall outcomes)

  DC becomes an option when medical management fails to control ICP. Surgical decompression can be done in combination with an evacuation procedure of a mass lesion, such as a subdural hematoma, or as a primary treatment for increased ICP. By removing part of the skull and allowing the edematous brain to expand outward, DC can immediately lower ICP and potentially improve survival in selected cases. However, its indications, timing, and long-term neurological impact in pediatric populations remain subjects of ongoing debate. Decompressive craniectomy will be discussed in detail in the subsequent chapter.[37][44]

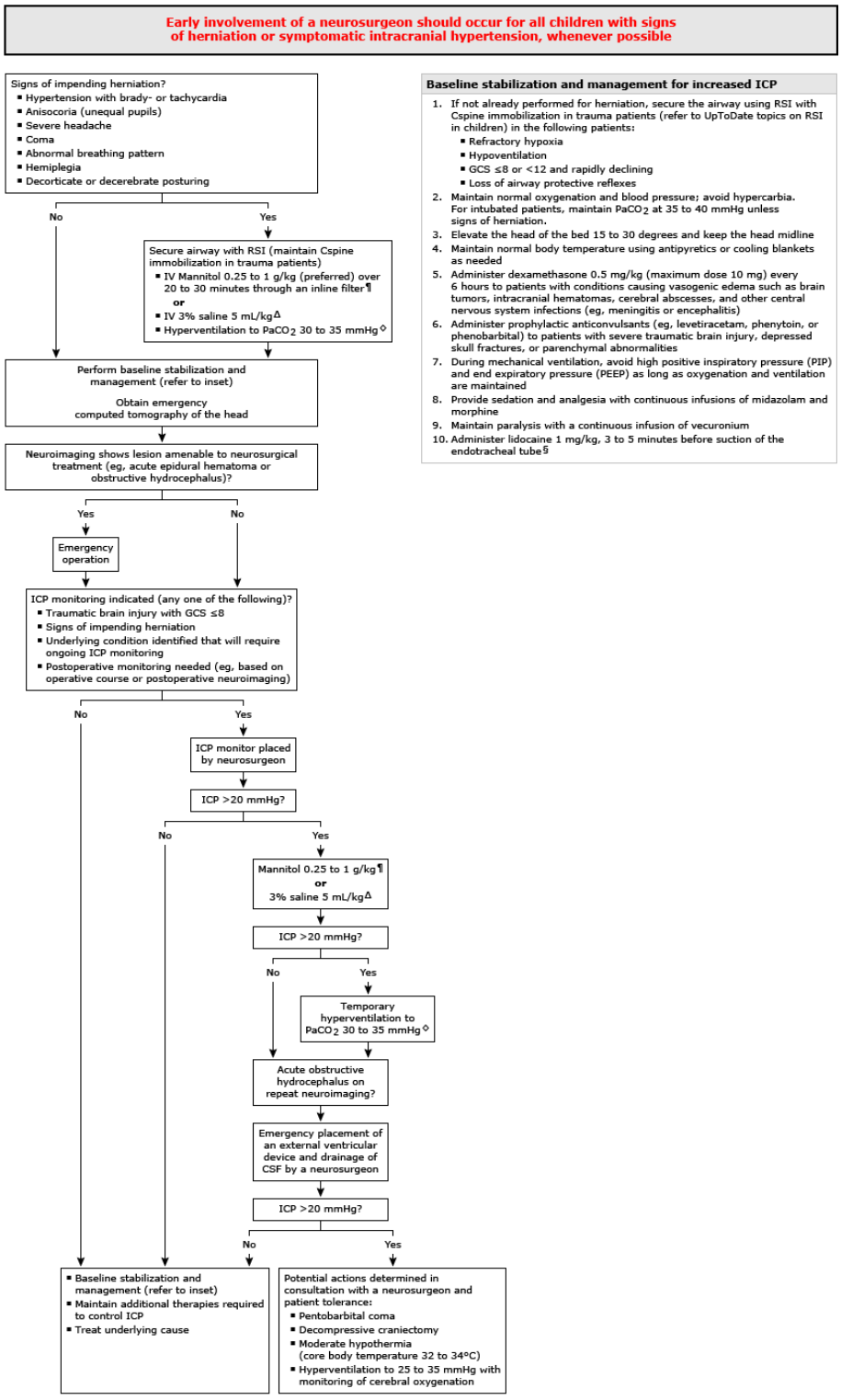


Figure 6 - Treatment of acute brain herniation or symptomatic intracranial hypertension (ICP >20 mmHg [27 cm H20]) in children[46]

Table 5 - Current Status of Pediatric Traumatic Brain Injury Guidelines[37]

Topic	Recommendations	Direct/Indirect/ Treatment Series	Ongoing Research
Hyperosmolar therapy	For ICP control Level II 1. Bolus hypertonic saline (3%) is recommended in patients with intracranial hypertension. Recommended effective doses for acute use range between 2 and 5 mL/kg over 10–20 min. For ICP control Level III 1. Continuous infusion hypertonic saline is suggested in patients with intracranial hypertension. Suggested effective doses as a continuous infusion of 3% saline range from between 0.1 and 1.0 mL/kg of body weight per hour, administered on a sliding scale. The minimum dose needed to maintain ICP < 20 mm Hg is suggested. 2. Bolus of 23.4% hypertonic saline is suggested for refractory ICP. The suggested dose is 0.5 mL/kg with a maximum of 30 mL.	9 Direct studies 3 Class 2, 6 class 3 2 RCTs 1 Prospective 5 Retrospective 1 Treatment series	ADAPT hypotheses • Hyperosmolar therapies improve outcomes. • Hypertonic saline is more effective than mannitol for ICP control.
Analgesics, sedatives, and neuromuscular blockade	For ICP control Level III 1. With use of multiple ICP-related therapies, as well as appropriate use of analgesia and sedation in routine ICU care, avoiding bolus administration of midazolam and/or fentanyl during ICP crises is suggested due to risks of cerebral hypoperfusion.	6 Studies All class 3 1 Direct prospective 1 Indirect prospective 2 Direct retrospective 2 Direct treatment series	None known
CSF	For ICP control Level III 1. CSF drainage through an external EVD is suggested to manage increased ICP.	5 Studies All class 3 1 Direct retrospective 3 Direct treatment series 1 Indirect treatment series	ADAPT hypotheses • Continuous CSF drainage improves outcomes. • Continuous CSF drainage reduces other ICP therapies.
Ventilation	To improve overall outcomes Level III 1. Prophylactic severe hyperventilation to a $Paco_2$ < 30 mm Hg in the initial 48 hr after injury is not suggested. 2. If hyperventilation is used in the management of refractory intracranial hypertension, advanced neuromonitoring for evaluation of cerebral ischemia is suggested.	2 Studies Both class 3 1 Indirect retrospective 1 Direct treatment series	ADAPT hypotheses • Prophylactic hyperventilation (Co_2 < 30 mm Hg) is associated with unfavorable outcomes. • Moderate hyperventilation is associated with favorable outcomes.
Barbiturates	For ICP control Level III 1. High-dose barbiturate therapy is suggested in hemodynamically stable patients with refractory intracranial hypertension despite maximal medical and surgical management.	4 Direct studies All class 3 1 Retrospective 3 Treatment series	None known
DC	For ICP control Level III 1. DC is suggested to treat neurologic deterioration, herniation, or intracranial hypertension refractory to medical management.	23 Direct studies All class 3 1 RCT 1 Prospective 5 Retrospective 16 Treatment series	None known

1.5 Decompressive Craniectomy

1.5.1 Historical Background and Theoretical Rationale

Decompressive craniectomy consists in removing a portion of the skull and opening of the underlining dura to allow the swollen brain to expand outward, thereby reducing ICP. The removed bone flap may be preserved for later cranioplasty. Although DC has been employed for over a century, with alternating phases of glory and oblivion, its role remains controversial, particularly in pediatric populations.

Historically, the earliest evidence of skull trephination dates to the Neolithic period and was discovered by the study of the French Prunières and Peruvian skull collections.[47] Trephination (also known as trepanning or burr holing) is a surgical procedure involving the creation of a hole in the skull. The origin of the term may come from multiple sources, one of which is the Greek word *trepanum*, literally meaning "borer" or "auger".[48] In fact, the practice of trephination was well-described during the Greek Era by Hippocrates and during the Roman Empire Era by Galen, who suggested its use for different types of skull fractures and other cranial bone abnormalities. Following a period of decline of popularity of such procedure, in 1518 the Italian physician and teacher of Anatomy at the University of Bologna, Berengario da Carpi, wrote the *Tractatus de fractura calve sive cranei*, giving the first description of craniotomy and the surgical instruments to perform it (*Fig. 7*). Hemicraniectomy was first described by Charles Adrien Marcotte in his thesis *De L'hemicraniectomie Temporarie* (1896), although at the time it wasn't used to treat severe TBI, the technique was demonstrated to decrease ICP. Finally, in 1901 Dr. Theodor Kocher reported the use of DC for patients with raised ICP following TBI in his manuscript *Hirnerschütterung, Hirndruck und chirurgische Eingriffe bei Hirnkrankheiten* (in English "Concussion, Intracranial Pressure and Surgical Procedures for Brain Diseases"). Inspired by Kocher lessons in Bern, the American neurosurgeon Cushing decided to adopt DC for the treatment of other brain disorders, such as brain tumors (1905). Three years later he studied the role of DC for treating the complications of bursting and penetrating brain injuries in World War I.

After the first half of the XX century the use of DC as standard practice to reduce intracranial pressure felt into discredit and only few studies were performed on the topic. In particular, in 1976 Cooper et al. recognized that the value of DC was

restricted to “those patients who enter hospital, obtunded but without demonstrable brain stem dysfunction, only to deteriorate subsequently because of increasing hemispheric edema and/or subdural clot”[49]. Thus, DC was deemed as second-tier treatment.

The improvement of ICP monitoring and of ICP-lowering medical therapies of the subsequent years only improved the application of DC to selected cases. Gower et al. (1988) demonstrated that treatment of ICP had to be guided by ICP values and the efficacy of DC after medical treatment had failed. Further studies[50][51] confirmed its utility in the management of refractory intracranial hypertension following severe TBI, although there was no great evidence on a significant improvement of the functional status of the patient. However, an important consideration to make is that at that time no randomized control trials (RCT) had been performed. From the start of the XXI century until now, only two RCT have been carried on, the DECRA trial and RESCUEicp trial, none of which is specific for the pediatric population.[52]

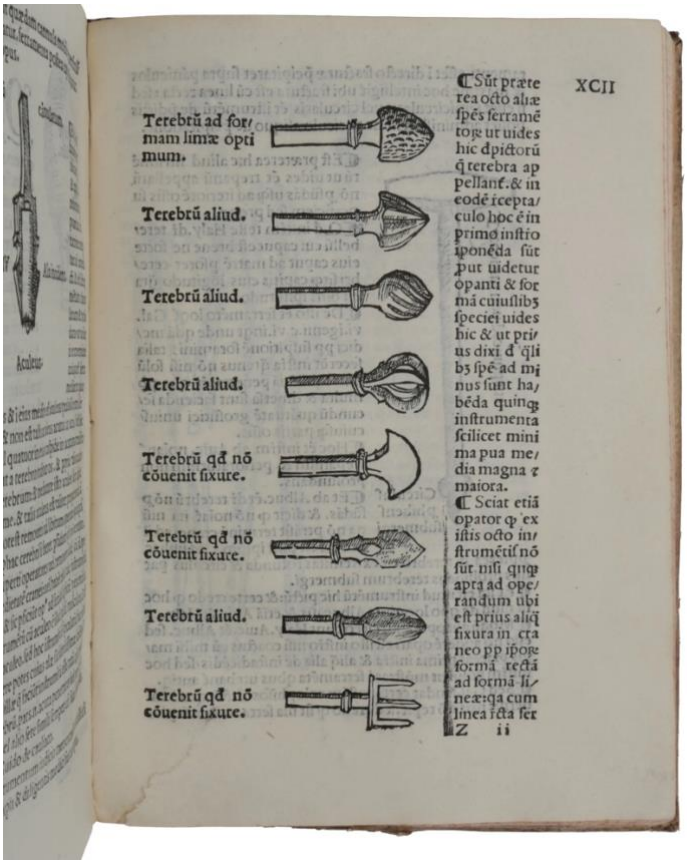
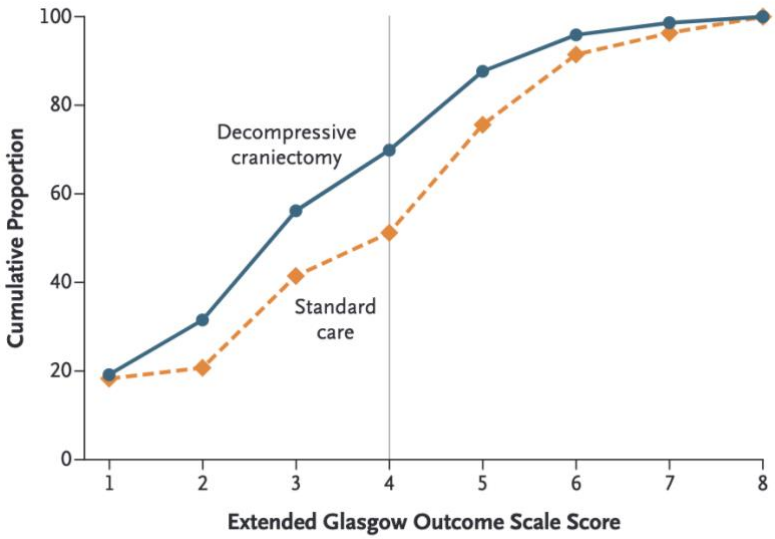


Figure 7 – “De Fractura Calvae sive Cranei”, original Italian translated copy (from Vittorio Putti, Berengario Da Carpi “De Fractura Calvae sive Cranei”, Bologna—L. Cappelli Editore, 1937, private collection.[52]

1.5.2 Evidence from Clinical Trials: DECRA and RESCUEicp

Two major RCTs have evaluated the efficacy of DC in adults: the DECRA and RESCUEicp trials. The 2011 DECRA trial (from December 2002 through April 2010) studied 155 patients between the ages of 15 and 59 years, who had severe, non-penetrating TBI and early refractory ICP (>20 mmHg for more than 15 minutes and within one hour, despite treatment for ICHTN). These patients were randomized, within 72 hours from the injury, to undergo bifronto-temporoparietal decompressive craniectomy plus standard medical care (73 patients) or continue medical care alone (82 patients). Although the surgical group demonstrated reduced mean ICP and shorter duration of both ICU stays and ventilatory support, they had worse neurological outcomes as measured by the Extended Glasgow Outcome Scale (*Graph 1*).[53]



Graph 1 – DECRA trial: Cumulative Proportions of Results of the Extendend Glasgow Outcome Scale: According to this measure, an unfavorable outcome occurred in 70% of patients in the craniectomy group and 51% of those in the standard-care group (P=0.02).[53]

The RESCUEicp trial (from January 2004 through March 2014) later investigated DC as a last-tier treatment in 408 patients between 10 and 65 years of age, with refractory raised ICP (>25 mmHg for 1–12 hours), despite first and second-tier therapies (*Fig. 8*). Participants were randomly assigned to undergo either hemicraniectomy or bifrontal craniectomy with medical therapy (202 patients), or to continue medical therapy and the possibility to add barbiturates

when needed (196 patients). Results showed reduced 6-month mortality in the surgical group compared to the medical one (26.9% vs 48.9%), but with higher rates of vegetative state and severe disability. Rates of favorable outcomes (moderate disability and good recovery) were similar between the two groups.[54]

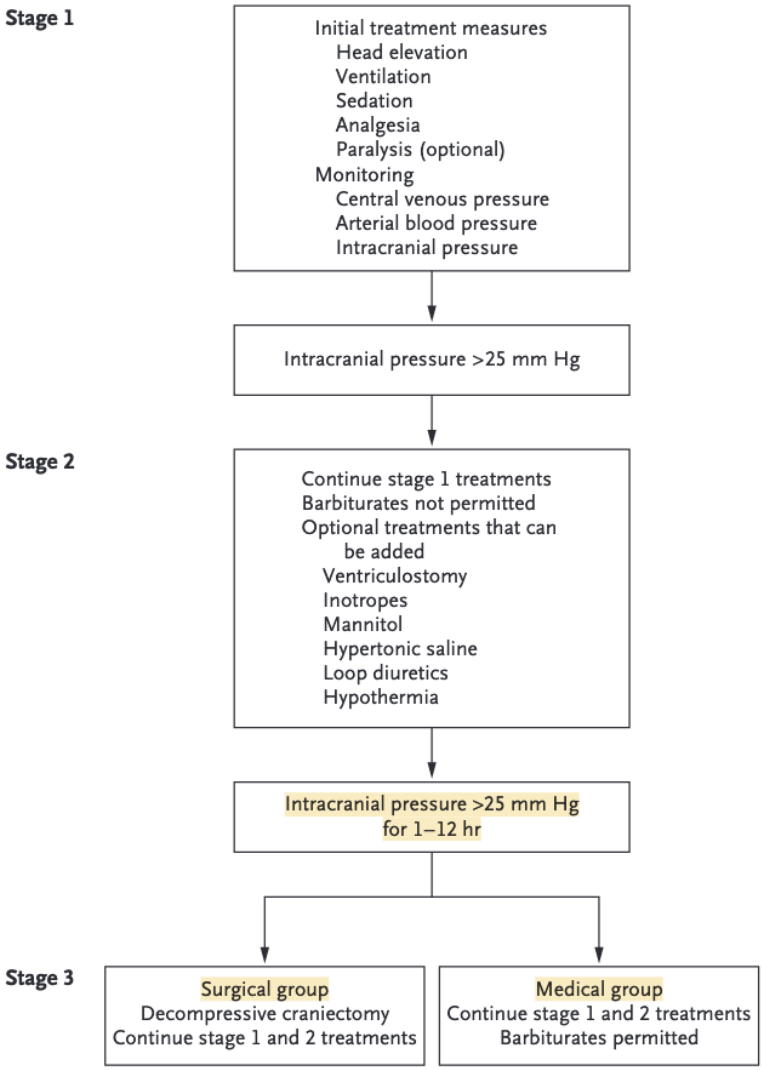


Figure 8 – RESCUEicp trial: Stages of Therapeutic Management[54]

The DECRA trial aimed to assess the effectiveness of early DC, so as second-tier therapy, for moderate ICHTN in patients with diffuse TBI. Instead, the goal of the RESCUEicp trial was to assess the effectiveness of decompressive craniectomy as salvage treatment, meaning as last chance. These findings suggest that while DC is effective in controlling ICP and reducing mortality, it does not necessarily improve long-term neurological outcomes. Thus, neither of them, together or taken singularly, provide definitive evidence in favor or against performing

decompressive craniectomy. Instead, the key message we can retrieve from these studies, is that potential benefits and complications should always be balanced and weighted on a case-by-case basis. In the pediatric setting, evidence remains largely observational, and no RCTs to date have definitively established DC utility.

1.5.3 Indications and Current Recommendations

Decompressive craniectomy, as mentioned before, is currently recommended as a salvage therapy for intracranial hypertension refractory to maximal medical management in both adult and pediatric populations[37]. Although evidence in children remains limited to class III studies and observational cohorts, the 2020 Update of Decompressive Craniectomy Recommendations by the BTF suggest DC for neurologic deterioration, clinical or radiological signs of herniation, or sustained elevated ICP (>20–25 mmHg), when first- and second-tier interventions fail.[55]

A key distinction must be drawn between primary and secondary DC:

- Primary DC is performed prophylactically at the time of surgical evacuation of a mass lesion (e.g. hematoma, contusion), often in anticipation of brain swelling. This can be either therapeutic, to address brain swelling, or prophylactic, to prevent anticipated edema.
- Secondary DC, instead, is conducted later in the clinical course, typically in the ICU, when ICP remains elevated despite exhaustive medical treatment.[56]

The updated BTF Guidelines (2020) have integrated in the overall body of evidence the RESCUEicp and DECRA trials, which implied the introduction of the following new recommendations:

Level IIA – to improve mortality and overall outcome

1. *NEW – Secondary DC performed for late refractory ICP elevation is recommended to improve mortality and favorable outcomes.*
2. *NEW – Secondary DC performed for early refractory ICP elevation is not recommended to improve mortality and favorable outcomes*.*
3. *A large frontotemporoparietal DC (not less than 12 × 15 cm or 15 cm in diameter) is recommended over a small frontotemporoparietal DC for reduced mortality and improved neurological outcomes in patients with severe TBI.*

** This recommendation should not be extrapolated to primary DC.*

Level IIA – for ICP control

4. *NEW – Secondary DC, performed as a treatment for either early or late refractory ICP elevation, is suggested to reduce ICP and duration of intensive care, though the relationship between these effects and favorable outcome is uncertain.*

Of the new Level IIA recommendations, the first one relates to the positive findings of the RESCUEicp trial, while the second one to the negative results taken from the DECRA study.[53][54]

The evidence used for postulating these recommendations is mainly based on the adult population, thus it cannot be directly applied to the pediatric one.

Instead, the Third Edition of the Brain Trauma Foundation Guidelines for the Management of Pediatric Severe TBI (2019), specifically address the pediatric context and offers a more tailored, although still prudent, approach. They give a Level III recommendation, stating that DC in children is suggested to treat neurologic deterioration, herniation, or intracranial hypertension refractory to medical therapy. The guidelines emphasize that the overall quality of evidence for this topic is low. Therefore, decisions must be based on individual patient evaluation and institutional expertise.

1.5.4 Description of the technique

The surgical technique itself varies significantly between institutions, but several key elements are broadly accepted to optimize decompression:

- The bone flap should measure at least 10–12 cm in diameter and extend to the temporal squama, parietal convexity, and frontal lobe—a configuration referred to as frontotemporoparietal hemicraniectomy.[57] Some surgeons advocate a bifrontal DC in diffuse brain swelling without lateralization.[58]
- Temporal bone removal is critical in mitigating the risk of uncal herniation, and decompression should extend to the floor of the middle cranial fossa.[59]
- Durotomy, i.e. opening of the dura mater, is necessary in most cases to achieve sufficient volume expansion. Techniques range from no

manipulation, simple slit incisions or wide duraplasty using autologous or synthetic grafts.[37]

- The bone flap is stored (in sterile conditions, subcutaneously in the abdomen, or in cryopreservation) for future cranioplasty once swelling resolves.[60]

In this part the description of a decompressive hemicraniectomy will follow.

The patient is positioned supine with padding under the ipsilateral shoulder and pelvis to facilitate a 90° head rotation, minimizing cervical spine strain and optimizing venous outflow. Moderate elevation of the headpiece can further enhance venous drainage but should be cautiously adjusted to prevent excessive cervical traction. Rigid skull fixation is achieved using a three-point Mayfield head holder, ensuring stability and maximal operative exposure.

The incision begins at the midline near the widow's peak, following a curved trajectory behind the ear, terminating approximately two finger breadths posterior to the mastoid notch, avoiding extension below the mastoid tip to preserve the occipital artery. After standard shaving and draping, the skin is incised superficially at first, maintaining the integrity of the hypodermal plane where the occipital artery lies. The vessel is identified and spared through blunt dissection before proceeding with deeper layers. The skin flap, including the outer temporal fascia, is then dissected and retracted anteriorly with flexible hooks, taking care to protect the frontal branch of the facial nerve. The temporalis muscle is elevated using monopolar cautery or a Cobb elevator. A total of five burr holes are placed in standard locations: frontal, parietal, keyhole, posterior temporal squama, and near the lambdoid suture. These are connected using a craniotome to create a large fronto-temporoparietal bone flap, which is removed. If necessary, the minor sphenoid wing is thinned with a cutting drill and fractured to extend the exposure. The temporal squama is further removed using rongeurs, down to the middle cranial fossa base, spanning from the sphenoid wing anteriorly to the petrous portion of the temporal bone posteriorly.

The dura mater is opened in a stellate or cruciate fashion, though in emergency settings, rapid dural opening without duraplasty may be employed. Instead, in pediatric patients, duraplasty using autologous or synthetic materials is always performed to accommodate brain swelling and reduce the risk of complications

such as subdural hygromas and hydrocephalus. The surgery typically concludes with placement of two non-suction epidural drains, subcutaneous closure, skin stapling, and standard wound dressing.[61]

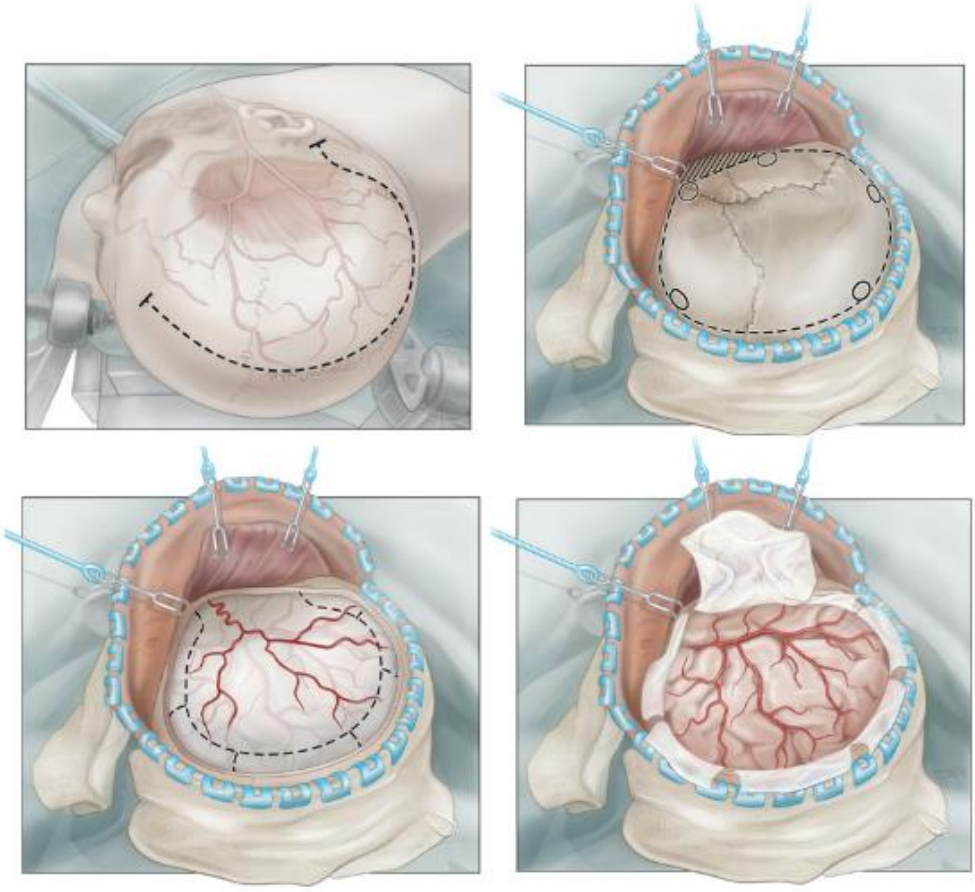


Figure 9 - Right-sided Decompressive Hemicraniectomy[61]

1.5.5 Controversies and Ethical Considerations in Pediatric DC

Despite its widespread adoption in severe TBI management, DC remains a controversial intervention. The controversy arises from several factors: the invasive nature of the procedure, absence of standardized indications, variability in surgical techniques, heterogeneous outcome reports, and the risk of significant complications such as infection, hydrocephalus, external cerebral herniation, and need for subsequent cranioplasty.[37]

In pediatric populations, the controversy is further compounded by the lack of robust evidence from randomized trials and the complex ethical considerations surrounding the procedure. While children have greater neuroplasticity and

potentially more favorable recovery, the long-term impact on neurodevelopment, quality of life, and functional independence remains uncertain.[62]

The decision to proceed with DC must therefore be individualized, considering the timing of the intervention, patient age, and family preferences and values. In clinical practice, these decisions are guided by a combination of neuroimaging findings, ICP measurements, and clinical deterioration, focusing on maximizing cerebral compliance and minimizing secondary brain injury.

1.5.6 Complications

DC in pediatric patients is associated with a broad spectrum of complications, many of which mirror those observed in adult populations, although with age-dependent variations in prevalence and pathophysiological mechanisms.

Gopalakrishnan et al.[62] categorizes the complications of decompressive craniectomy (DC) into early (within 4 weeks of surgery) and late (beyond 4 weeks), highlighting the importance of their temporal distribution in both diagnosis and management. Among early complications, the most clinically significant include hemorrhagic progression of contusions due to loss of the cranial tamponade effect, external cerebral herniation secondary to inadequate bone removal or duraplasty, cerebrospinal fluid leakage, postoperative infections, and early-onset seizures. These events often occur within the first week and necessitate close neuroimaging surveillance, particularly within the initial 48 hours. Late complications, more commonly observed after the first postoperative month, include subdural hygromas, hydrocephalus, and the Syndrome of the Trephined (SoT).

Subdural hygromas are frequently encountered and may evolve into hydrocephalus, particularly when accompanied by impaired CSF reabsorption.

Posttraumatic hydrocephalus, typically of the communicating type, is linked to factors such as a craniectomy margin close to the midline and prolonged CSF leakage.

The Syndrome of the Trephined, often underrecognized, is characterized by motor, cognitive, or behavioral deterioration due to atmospheric pressure gradients and altered cerebral perfusion beneath the cranial defect. Importantly, early cranioplasty—ideally within 12 weeks—is associated with a reduced incidence of hydrocephalus and SoT. The review emphasizes that the success of DC is closely

tied to meticulous surgical technique, sufficient decompression and prompt identification of delayed complications, underscoring the need for vigilant follow-up and individualized postoperative strategies to optimize long-term neurological outcomes.

A particularly relevant contribution to the understanding of pediatric-specific complications following decompressive craniectomy is provided by Martin et al.[63], who retrospectively reviewed the outcomes of autologous bone flap cranioplasty in a cohort of 27 pediatric patients treated for TBI. The study underscores the high incidence of postoperative complications, with a particular emphasis on bone flap resorption (osteolysis), which occurred in up to 81.8% of children under the age of 7. More than half of these cases (54.4%) necessitated surgical revision, highlighting the clinical significance of this complication in the youngest subpopulation.

Several factors were associated with an increased risk of resorption, including young age, large craniectomy surface area (≥75 cm^2), presence of ventriculoperitoneal shunts, and extensive duraplasty. The pathophysiology underlying this phenomenon may be linked to the unique osteogenic dynamics of the growing skull: in early life, cranial ossification is tightly regulated by the interaction between the dura mater and the overlying calvaria. The immature dura releases growth factors essential for osteogenesis, particularly during the period of rapid brain growth in the first two years of life. The authors suggest that expansile duraplasty using synthetic or allogenic grafts may disrupt this physiological signaling, leading to impaired bone reintegration and higher rates of osteolysis.

Infectious complications, in contrast, were found to be less frequent in younger children, with higher rates observed in adolescents and young adults (22.2% and 12.8%, respectively). Other postoperative issues included bone flap loosening, hematoma formation, and CSF leakage, though these were less prevalent.

The timing of cranioplasty also emerged as a potentially modifiable factor. Pediatric patients often undergo earlier reconstruction for cerebral protection and to accommodate cranial growth; however, this may inadvertently increase the risk of graft failure and infection. Taken together, these findings call into question the routine use of autologous bone reimplantation in very young patients and lend

support to the cautious consideration of synthetic alternatives, particularly when risk factors for resorption are present.

Among the most frequent postoperative complications are subdural hygromas and posttraumatic hydrocephalus. A prevailing hypothesis attributes the elevated rate of subdural collections in infants to the immaturity of the CSF resorption mechanisms, specifically the prominence of the dural venous plexus, which in early life may compensate for underdeveloped arachnoid granulations. According to this theory, expansile duraplasty, often performed using allogenic grafts, may interfere with native dural CSF absorption, predisposing the subdural compartment to fluid accumulation.

Posttraumatic hydrocephalus may exacerbate or perpetuate these collections, particularly when accompanied by arachnoidal tears sustained during trauma or surgical manipulation, facilitating direct CSF passage into the subdural space. Further contributing factors include blood–brain barrier disruption and altered CSF hydrodynamics, both of which may be induced by the primary injury, the surgical procedure, or their interplay. In a retrospective cohort study of 91,583 pediatric TBI patients, Bonow et al.[64] reported a significant association between delayed cranioplasty and hydrocephalus development (aOR 3.67), underscoring the protective role of timely skull reconstruction.[62]

The benefits of early cranioplasty, preferably within 12 weeks post-DC, are becoming increasingly recognized and include improved cerebral blood flow, neurocognitive recovery, and reduction in complications such as sunken flap syndrome and hydrocephalus.

Overall, the literature emphasizes the need for pediatric-specific management strategies to mitigate these complications. Ongoing research into biomaterials for cranioplasty, the ideal timing of bone flap reinsertion, and strategies for maintaining CSF dynamics post-DC will be crucial in refining care standards for this vulnerable population.

1.5.7 Outcomes

While decompressive craniectomy offers a critical survival benefit in pediatric patients with refractory intracranial hypertension, the long-term outcomes remain complex and variably reported, reflecting a spectrum ranging from full recovery to

severe disability. High-quality, large-scale studies are lacking, and current knowledge is derived predominantly from retrospective cohorts and single-center case series. Nonetheless, these studies offer important insights into both the neurological and functional trajectories of pediatric patients post-DC, as well as the spectrum of delayed complications that may influence recovery and quality of life.

A large multicenter retrospective cohort study by Bruns et al.[65], drawing from the Trauma Register DGU and encompassing over 2,500 pediatric patients from Germany, Austria, and Switzerland, offers significant insight into short-term outcomes following DC compared to standard medical management.

The study revealed that DC was performed in 16% of pediatric patients, with this subgroup generally presenting lower GCS scores, more severe injuries, and longer ICU stays. At ICU discharge, mortality was higher in the DC group (20.6%) compared to the medically managed cohort (13.7%), with an adjusted odds ratio of 1.20 (95% CI: 0.74–1.95). Similarly, poor neurological outcomes (defined as death or vegetative state) were more frequent in the DC group, with an adjusted odds ratio of 1.56 (95% CI: 1.01–2.40) after risk adjustment.

Importantly, the study underscores how age under six years, brain edema, and intracerebral hemorrhage significantly increased the odds of mortality and poor outcome. Conversely, CSF drainage and hematoma evacuation were independently associated with better outcomes, suggesting that in selected cases, these interventions may offer safer and more effective alternatives to DC.

Although the authors emphasize that DC may be lifesaving in certain contexts, especially in patients with AIS[1] head score of 5, where improved outcomes were seen—they caution against its routine use in the absence of high-quality evidence. The lack of long-term outcome data, variability in surgical timing and technique, and heterogeneity in patient selection all limit the generalizability of findings.

In a retrospective review by Nagy et al.[66], encompassing 47 pediatric cases treated over a decade, 75% of surviving patients achieved a favorable outcome, defined as a Glasgow Outcome Scale (GOS) score of 4 or 5 at six months post-

[1] Refers to the Abbreviated Injury Scale (AIS) specifically for head injuries. The AIS is a system for grading the severity of injuries, with scores ranging from 1 (minor) to 6 (currently untreatable).

procedure. These results are consistent with other reports in the literature, which show rates of favorable outcome ranging between 81% and 100% in selected cohorts.

Importantly, this study examined the impact of timing on outcomes, comparing acute (<24 hours) versus subacute (>24 hours) DC. Although the acute group presented with significantly lower Glasgow Coma Scale scores at admission, no statistically significant difference in GOS was observed at discharge or at six months between the two groups. This suggests that clinical status at presentation may guide the urgency of surgical decompression more appropriately than rigid temporal thresholds. Notably, mortality was 31.9%, a rate comparable to prior series, and complications occurred in 36.6% of patients, including infection, CSF leak, and subdural or subgaleal fluid collections. Yet, the incidence of post-traumatic hydrocephalus (PTH) was only 6.9%, considerably lower than the typically reported 21–40%. This reduction may be attributable to the standardized early use of external ventricular drains and subgaleal drains, as well as institutional preference for early cranioplasty, typically performed within four weeks of DC.

Overall, the findings suggest that early DC in pediatric TBI, when clinically indicated, can lead to favorable neurological recovery, especially when accompanied by a structured, protocol-based post-operative management strategy.

Nonetheless, a consistent pattern emerges across the literature: a non-negligible proportion of pediatric patients survive with favorable neurological outcomes, particularly when DC is performed early and in the absence of profound preoperative neurological impairment (e.g., bilaterally fixed pupils or low initial GCS). However, functional recovery is far from uniform. Many children develop persistent motor, cognitive, behavioral, or sensory deficits. These sequelae, though often less severe than in adult populations due to greater neuroplastic potential, may profoundly affect quality of life and neurodevelopmental trajectory. Furthermore, several delayed complications, such as posttraumatic hydrocephalus, subdural hygromas, bone flap resorption, and seizures, are common and may require additional surgical interventions, particularly in younger patients.

Long-term outcomes also appear to be influenced by age at the time of injury, with children over 5 years of age more likely to achieve meaningful recovery,

possibly reflecting more mature neurovascular and autoregulatory physiology. Conversely, infants and toddlers, who may lack reliable neurological signs and are at increased risk of CSF circulation disturbances, often face worse prognoses.

To conclude, decompressive craniectomy can be life-saving and occasionally function-preserving in pediatric patients with otherwise intractable intracranial hypertension. However, the procedure is not without cost, morbidity remains substantial, and the long-term trajectory of recovery is often complex and resource intensive. These findings underscore the urgent need for prospective, standardized, multicenter pediatric studies, not only to better delineate the indications, timing, and technical approach to DC in children, but also to understand how to optimize long-term functional, cognitive, and psychosocial outcomes.[67][68][69]

2 AIM OF THE STUDY

This study aims to retrospectively analyze the clinical outcomes of pediatric patients who underwent decompressive craniectomy at the Pediatric Neurosurgery Unit of the University Hospital of Padua, for both traumatic and non-traumatic brain injuries.

The primary objective is to evaluate the role of DC in neurological outcomes, both in the short and long term, and to identify clinical, radiological, and surgical factors potentially associated with recovery or with unfavorable prognosis.

To enhance the interpretative value of our findings and contribute to the broader understanding of pediatric DC, our institutional results were systematically compared with data from selected studies in the international literature.

3 MATERIALS AND METHODS

3.1 Study Design and Inclusion Criteria

A retrospective observational study was conducted at the Pediatric Neurosurgery Unit of the University Hospital of Padua, analyzing medical records of pediatric patients who underwent Decompressive Craniectomy between January 2012 and December 2024. Inclusion criteria comprised all patients under 18 years of age who received a primary or secondary DC for various acute intracranial pathologies, regardless of the underlying etiology.

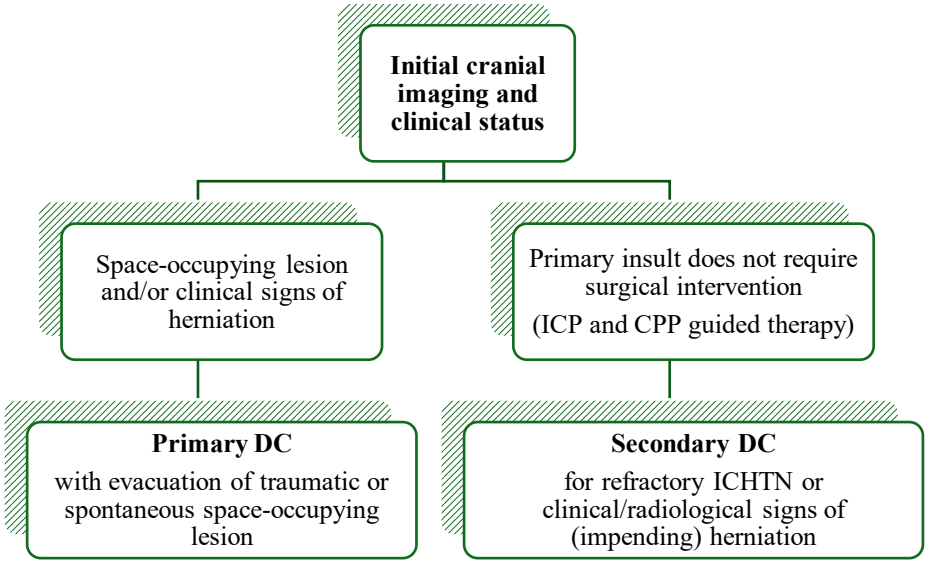


Figure 10 - Illustration of the therapeutic pathways for primary and secondary DC according to our institutional protocol

The decision to perform decompressive craniectomy was based on the combination of initial clinical status, neuroimaging findings, and ICP monitoring, in alignment with the Brain Trauma Foundation (BTF) guidelines.[37] Primary DC was performed in patients presenting with space-occupying lesions (e.g. traumatic hematomas or spontaneous hemorrhages) associated with clinical or radiological signs of herniation, in whom urgent decompression and lesion evacuation were deemed necessary. In contrast, secondary DC was indicated for patients with diffuse brain injury or non-surgical primary insults, who subsequently developed refractory intracranial hypertension despite maximal medical therapy, including sedation,

hyperosmolar therapy, and CSF drainage, with or without evolving signs of impending herniation.

Clinical and radiological data were extracted from patient electronic charts, the following variables were collected: sex, age at time of surgery, type of acute event leading to DC, indication for surgery (primary or secondary DC), underlying pathology, presence of comorbidities. Additional information included clinical presentation immediately prior to surgery, Glasgow Coma Scale (GCS) score at admission and pre-operative pupillary symmetry.

Neuroimaging findings were assessed through pre-operative and post-operative computed tomography (CT) scans and magnetic resonance imaging (MRI), including evaluation of midline shift (categorized as <5 mm or >5 mm), evidence of brain oedema and intracranial hematomas. Therapy data included the presence of Intracranial Pressure Monitoring, the duration of hospitalization and stay in the Pediatric Intensive Care Unit (PICU), and surgical data. Surgical procedures included craniotomy with direct bone flap reimplantation, decompressive craniectomy (hemicraniectomy or bifrontal craniectomy) with duraplasty, and secondary cranioplasty. Post-operative recovery was retrospectively assessed from the patient records of the routine clinical follow-up, immediately after surgery, at 30 days, 3 months and 6 months. Long-term functional outcomes were assessed using the Glasgow Outcome Scale - Extended Pediatric Version (GOS-E Peds). Data were collected through structured telephone interviews conducted with the legal guardians or primary caregivers of the pediatric patients. Interviews were carried out using a standardized questionnaire adapted for telephone administration, based on the format proposed by Wilson et al.[70] for the GOSE. Prior to initiating the interview, the interviewer provided a detailed explanation of the purpose of the study and obtained verbal informed consent to proceed. Participants were reassured about confidentiality and informed that participation was voluntary and would not affect the patient's medical care. All interviews were conducted at least 6 months post-injury, ensuring the assessment reflected a long-term outcome and not temporary postoperative conditions. Loss to follow-up occurred when patients changed the clinical care center. Secondary outcome parameters were defined as the development of complications, especially those associated with the surgical

intervention, together with timing from craniectomy to cranioplasty and type of cranioplasty (autologous vs custom-made).

Table 6 - Overview of the Criteria for the GOSE Categories[71]

GOS 5-point scale	*GOSE 8-point scale*	*Domain*	*Criteria*
Dead	1. Dead		
Vegetative State	2. Vegetative State	Consciousness	
Severe Disability (SD) Conscious but dependent	3. Lower SD	Function in Home	Unable to look after themselves for 8 h
	4. Upper SD	Function in Home Function Outside the Home	Unable to look after themselves for 24 h OR Unable to shop OR Unable to travel
Moderate Disability (MD) Independent but with limitations in one or more activities	5. Lower MD	Work/Study Social and Leisure Activities Family and Friendships	Unable to work/study OR Unable to participate OR Constant problems
	6. Upper MD	Work Social and Leisure Activities Family and Friendships	Reduced work capacity OR Participate much less OR Frequent problems
Good Recovery (GR) Return to normal life	7. Lower GR	Social and Leisure Activities Family and Friendships Symptoms	Participate a bit less OR Occasional problems OR Some symptoms affecting daily life
	8. Upper GR		No problems

The GOSE categorization (ranging from 1=Death to 8=Upper Good Recovery) was based on the responses provided regarding the patient's independence, ability to resume daily and school activities, neurological symptoms, and psychosocial functioning at the time of follow-up. When uncertainty emerged during classification, additional probing questions were used to clarify the level of disability or recovery.

3.2 Systemic Review of the Literature

To contextualize the present study within the broader body of existing scientific evidence on decompressive craniectomy in pediatric patients, a systematic review of the literature was performed. Given the predominance of retrospective series and case reports in the pediatric population, this review of the literature was conducted to identify relevant studies that evaluate the indications, outcomes, complications, and long-term prognosis of DC in children with intracranial hypertension.

A systematic search was performed according to PRISMA guidelines[72]. The databases consulted included PubMed, EuropePMC and ResearchGate. The search strategy combined the following MeSH terms and keywords: "decompressive craniectomy" OR "decompressive surgery", "pediatric" OR "children" OR

“infants” AND “traumatic brain injury” OR “intracranial hypertension” OR “refractory ICP”.

The inclusion criteria were:

- Original studies (RCTs, cohort studies, case series) reporting clinical outcomes in pediatric patients (<18 years) undergoing DC;
- Studies published in English;
- Studies providing details on indications, surgical technique, complications, and follow-up.

Exclusion criteria included:

- Reviews, editorials, conference abstracts;
- Studies involving only adult patients;
- Lack of relevant data;
- Studies published more than 10 years ago.

Most studies described DC as a second-tier intervention in the context of severe traumatic brain injury, refractory intracranial hypertension, or malignant cerebral edema. Reported indications often included sustained ICP > 20–25 mmHg, radiological signs of impending herniation, or failure of maximal medical therapy.

Clinical outcomes were highly heterogeneous, with some series reporting favorable recovery in younger patients, especially when early DC was performed before clinical deterioration. However, several studies highlighted the uncertainty regarding long-term neurological outcomes, the high rate of complications and the lack of consensus on standardized surgical technique and timing.

3.3 Statistical Analysis

The statistical analysis aimed to explore potential associations between preoperative, perioperative, and postoperative variables and two primary endpoints: the presence of postoperative complications, and the functional outcome at follow-up, measured using the GOSE-Peds. The overall objective was to identify clinical, radiological, and surgical factors that might serve as early predictors of prognosis or perioperative morbidity in pediatric patients undergoing decompressive craniectomy.

Given the limited sample size (n=11), a purely descriptive and exploratory statistical approach was adopted. All analyses were performed using RStudio (Version 2024.12.1+563).

3.3.1 Descriptive Statistics

Continuous variables (e.g., age, GCS at admission, midline shift in mm, PICU stay, timing of cranioplasty in days) were summarized using mean and standard deviation (SD) when normally distributed, and median with interquartile range (IQR) when data showed skewed distributions or ordinal scaling. Categorical variables (e.g., sex, etiology, type of DC, presence of brain edema, pupillary symmetry, use of ICP monitoring, comorbidities, complications) were reported as absolute counts and proportions.

3.3.2 Comparative Analysis

To assess factors potentially associated with the occurrence of any complications (including CSF leakage, wound infection, hygroma, hydrocephalus, or bone flap resorption), univariate comparisons were conducted between patients with and without complications:

Fisher's Exact Test was used for comparisons between categorical variables (e.g., sex, etiology, type of DC, ICP monitoring, brain edema, pupillary symmetry, comorbidities), as it is robust for small samples and 2x2 contingency tables.

For continuous and ordinal variables (e.g., age, GCS, midline shift), the Mann–Whitney U test was used to compare medians between groups.

Patients were also stratified into two groups based on neurological outcome at follow-up: *favorable outcome* (GOSE-Peds ≥ 6), *unfavorable outcome* (GOSE-Peds < 6). Using this binary classification, a comparative analysis was made.

Spearman's rank correlation coefficient (ρ) was calculated between GCS and GOSE, due to the ordinal nature of GOSE and the small sample size. A strong positive correlation was observed, which was graphically represented using a scatterplot with fitted regression line.

Associations between other categorical predictors (e.g., traumatic vs non-traumatic etiology, primary vs secondary DC, isocoria vs anisocoria, presence of

ICP monitoring, presence of complications) and GOSE outcomes were tested using Fisher's Exact Test.

Continuous predictors such as age, timing of cranioplasty, and PICU (Pediatric Intensive Care Unit) length of stay were compared across outcome groups using Mann–Whitney U test, depending on distributional properties.

Visual inspection of relationships was an integral part of the analysis. In particular, graphical tools were employed using Excel. Scatterplots with regression lines were used to show the relationship between GCS and GOSE. Boxplots were generated to illustrate the distribution of GOSE scores in relation to pupillary symmetry, brain edema, and midline shift.

3.3.3 Data Cleaning and Handling of Missing Values

Non-numeric entries (e.g., '/' or "NA" fields) in columns were excluded or replaced by appropriate imputation (when justified) to avoid distortion of central tendency values. Each analysis was performed on complete-case data for the variables of interest.

3.3.4 Rationale for Variable Selection

The variables included in the analysis were chosen based on their clinical relevance, availability in the dataset, and established or suspected prognostic value from prior literature. For example, GCS at admission, pupillary response, and midline shift are well-established markers of injury severity. Brain edema and ICP monitoring reflect the pathophysiology and management of intracranial hypertension.

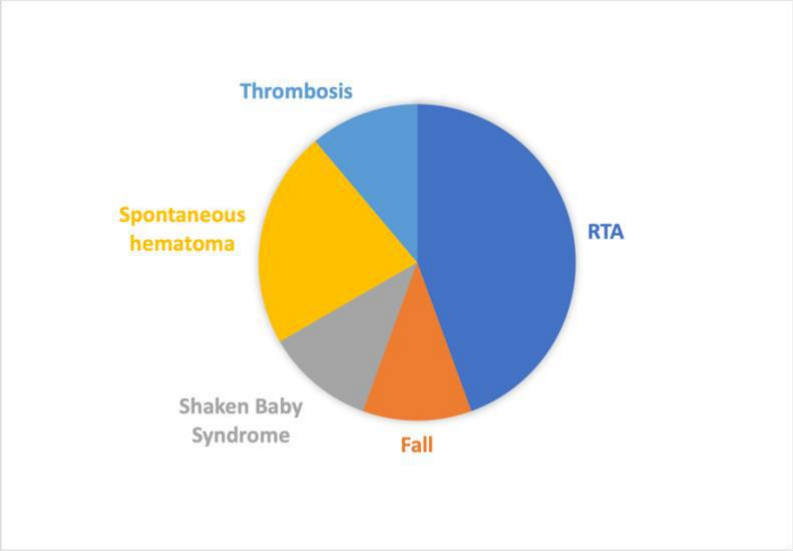
Comorbidities and etiology (traumatic vs non-traumatic) may impact both surgical risk and long-term outcome. Type of DC (primary vs secondary) and timing of cranioplasty were included due to their debated role in influencing recovery and complication rates.

4 RESULTS

4.1 Institutional Case Series

4.1.1 Demographics and Baseline Characteristics

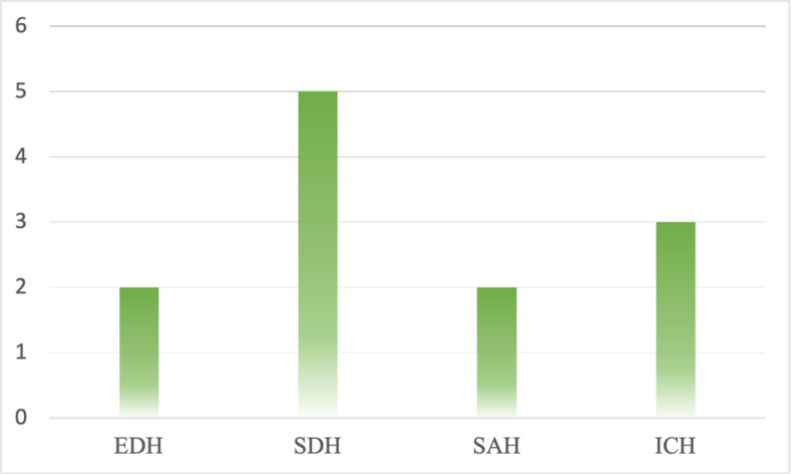
At the Pediatric Neurosurgery Unit of the University Hospital of Padua, between January 2012 and December 2024, a total of 11 patients, aged between 2 months and 13 ± 4 years (median 7,6; mean 6,8 ± 4), underwent decompressive craniectomy for both traumatic and non-traumatic etiologies. Of these patients, 3 were males (27,3%) and 8 were females (72,7%). The etiology leading to surgery was comprehensively grouped in two categories: traumatic (55,6%) and non-traumatic (44,4%) brain injuries (Graph 2). Among the traumatic brain injuries, 4 cases were due to road traffic accidents (RTA), 1 case due to falling from a tree and 1 case associated with Shaken Baby Syndrome. On the other hand, the non-traumatic brain injuries were caused by a spontaneous raise in ICP, associated to spontaneous extradural and subdural hematoma (n=3) and spontaneous thrombosis of the cerebral venous sinuses (n=1).



Graph 2 - Etiology

Primary DC, with evacuation of traumatic or spontaneous space-occupying lesion, was performed in 8 cases, secondary DC in 3 cases. All craniectomies were hemicraniectomies with duraplasty.

Urgent CT findings showed development of different types of brain injuries (*Graph 3*). Among these 2 were epidural hematomas, 5 subdural hematomas, 2 subarachnoid hemorrhages and 2 intracranial hemorrhages.



Graph 3 - Types of brain injuries

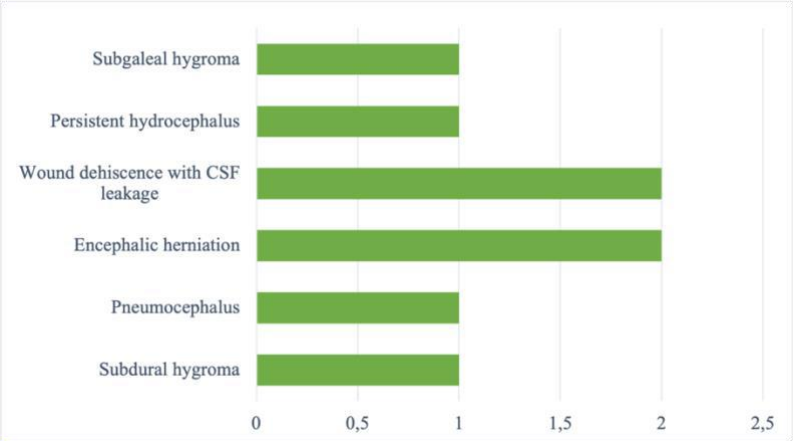
Midline shift was reported > 5 mm in the majority of patients (70%), instead only 40% of patients showed < 5 mm midline shift at pre-operative imaging. Brain edema was radiologically or intraoperatively confirmed in 8 cases.

Pre-operative GCS ranged from 3 to 15 (mean 7,1 ± 4, median 6)), with 7 patients presenting with a GCS ≤ 6. Pupillary reactivity was examined upon admission, and it was found that anisocoria (pupillary asymmetry), was present in 7 cases, of which 3 had fixed, nonreactive pupils. Whereas 4 patients showed isocoria (pupillary symmetry) and only one of them had normally reactive to light reflex pupils.

ICP monitoring via placement of a parenchymal or external ventricular catheter was performed in 6 patients, while it was not applied or documented in 5 patients.

All patients were admitted to the Pediatric Intensive Care Unit (PICU) following surgery. PICU stay ranged from 9 to 81 days, with a mean duration of approximately 28,8 days.

Postoperative complications were reported in 6 patients, with diverse presentations including central venous catheter (CVC) infection, epileptic encephalopathy and positive hemoculture. Neurosurgical-specific complications were noted in 5 cases, including cases of CSF leakage and wound dehiscence, subdural and subgaleal hygromas, refractory hydrocephalus, which was treated with a ventriculoperitoneal shunt, pneumocephalus and encephalic herniation (*Graph 4*).



Graph 4 - Neurosurgical-specific complications

Cranioplasty timing varied widely across the cohort, ranging from 16 days to 184 days post-DC, with a median of over 2 months (81 days). One patient did not undergo cranioplasty due to early mortality. The repositioned bone flap was either autologous (n=8) or custom-made (n=2).

4.1.2 Case reports

Traumatic Brain Injury: M, 6 y.o.

A 6-year-old boy with a history of autism spectrum disorder, moderate intellectual disability, and severe language delay was involved in a high-speed car accident while unrestrained in the back seat. Following a rear-lateral collision, he was found unconscious, displaced to the opposite side of the vehicle. On arrival of emergency services, he presented with a GCS score of 9/15 and exhibited rapid neurological decline, prompting on-site intubation after sedation and paralysis. During transfer, he remained hemodynamically stable.

At admission to the Emergency Department, he was intubated and immobilized with a cervical collar and spinal board. He exhibited a bleeding lacerated wound (~3 cm) in the right parietotemporal region with extrusion of brain tissue. Clinical examination showed preserved right-sided motor activity but absent movement on the left.

A total-body CT scan demonstrated a depressed skull fracture in the right temporoparietal region, associated with hemorrhagic parenchymal contusion, subarachnoid contamination, early uncal herniation, and a mild midline shift (*Image 1*). Neurosurgical evaluation confirmed the need for emergent decompression.

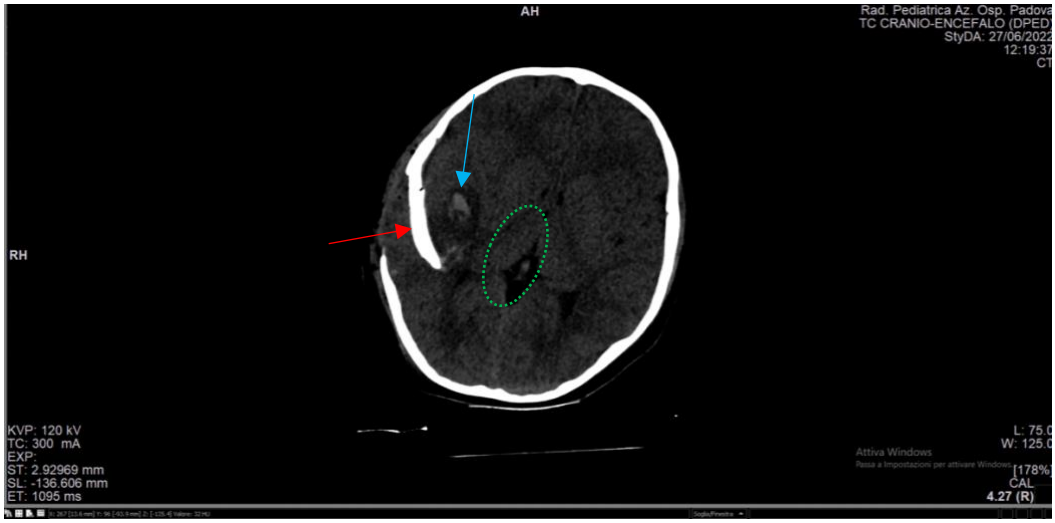


Image 1. Pre-operative CT scan showing depressed skull fracture in the right temporoparietal region (red arrow), associated with hemorrhagic parenchymal contusion (blue arrow), subarachnoid contamination, early uncal herniation, and mild midline shift (dashed green).

The patient underwent a right frontotemporoparietal decompressive craniectomy. Intraoperatively, the depressed bone fragment was found embedded in the brain (*Images 2 and 3*), which appeared edematous and actively bleeding. After bone removal, a branch of the right middle cerebral artery (M4) was identified as the source of arterial bleeding and was coagulated. A dural opening was performed, and an intraparenchymal ICP monitor was placed (initial ICP 6 mmHg). Hemostasis was achieved, and duraplasty completed using Lyoplant and fibrin glue. Total intraoperative volume replacement included 530 ml of blood, 500 ml of 5% albumin, and 1100 ml of crystalloids. Post-operative CT confirmed decompression, stable midline shift, persistent minimal uncal herniation, and no procedural complications, though a few residual bone fragments were suspected (*Image 4*).

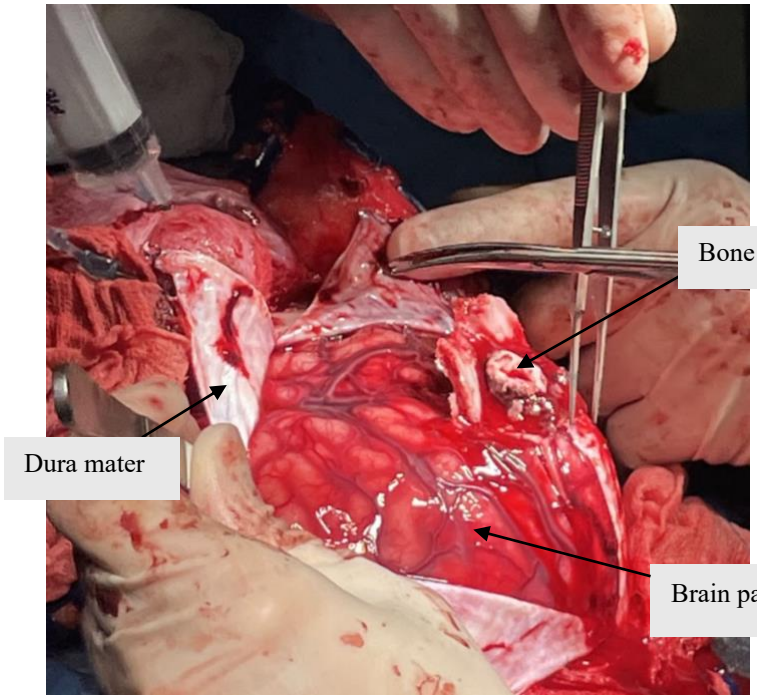


Image 2. Intraoperative image showing the edematous and hemorrhagic brain, in which is embedded the bone fragment.

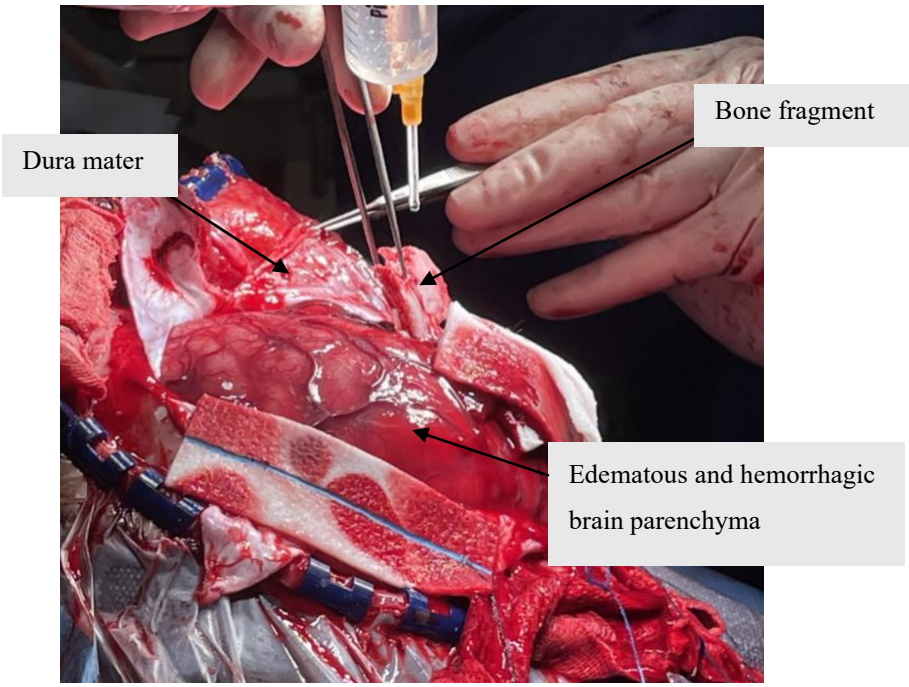


Image 3. Intraoperative image showing removal of bone fragment

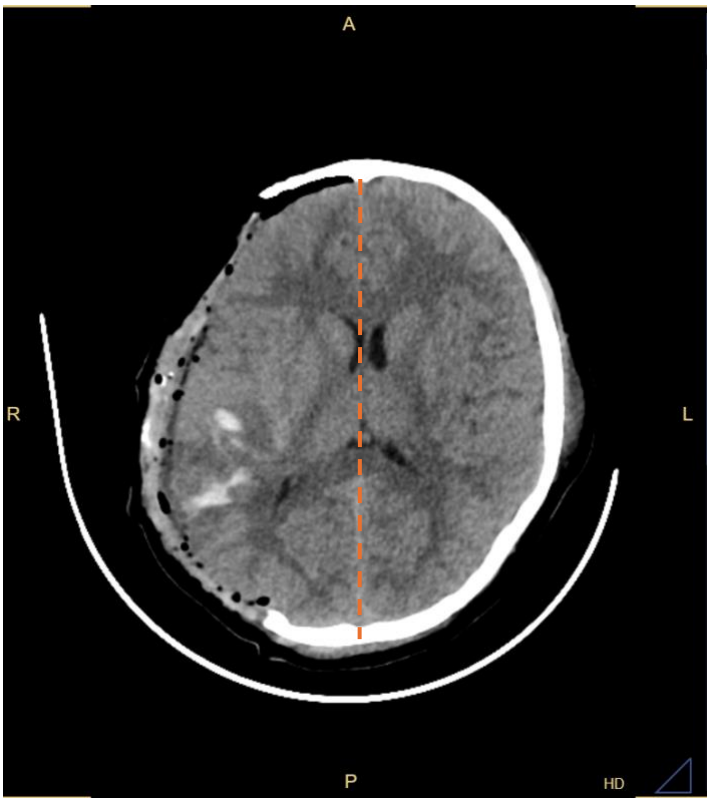


Image 4. Post-operative CT scan showing recovery of midline symmetry and successful decompression.

On awakening, the patient exhibited a left-sided hemiparesis, which showed progressive improvement in the following days. Due to rising inflammatory markers, empirical antibiotic therapy with ceftriaxone and vancomycin was

initiated, temporarily suspended after normalization, and subsequently reintroduced following renewed elevation. Blood cultures grew *Bacillus cereus* and *Staphylococcus epidermidis*. Serial imaging (MRI and CT) confirmed gradual resolution of the contusional hemorrhage and stability of the clinical condition.

With normalization of inflammatory markers, the child was transferred to the Pediatric Surgery Unit for continued management and planning of cranioplasty. He eventually underwent autologous bone flap repositioning reinforced with a synthetic substitute (Norian), without complications (*Image 5*).

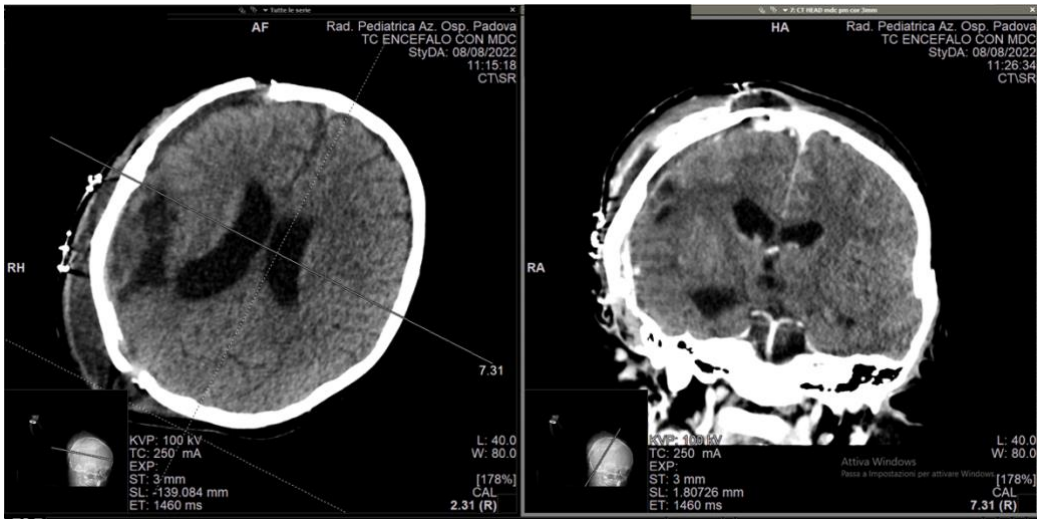


Image 5. Post-cranioplasty CT scan showing reconstruction with autologous bone flap.

At discharge, the patient was awake, alert, and interactive, with no focal cranial nerve or motor deficits, and walked without pathological gait patterns.

At follow-up, he demonstrated full ambulatory autonomy and no residual motor deficits, continuing his course of speech and motor rehabilitation.

Non-traumatic Brain Injury: F, 10 y.o.

A 10-year-old girl with a known history of chronic immune thrombocytopenia (ITP), presented with progressively worsening headache and repeated vomiting. Despite multiple emergency department evaluations and an initial brain MRI reported as normal, she subsequently experienced an acute symptomatic seizure. The event featured loss of consciousness, ocular revulsion, perioral cyanosis, hypersalivation, and generalized tonic-clonic activity, followed by postictal left facial deviation and hemiparesis.

Neuroimaging revealed thrombosis of the right transverse and sigmoid sinuses, with involvement of the superficial vein of Labbe, and a right temporal hemorrhagic venous infarction exerting mass effect on the right lateral ventricle. Although the midline structures were initially preserved, clinical deterioration and follow-up CT imaging demonstrated increasing cerebral edema and the appearance of a midline shift (*Image 6*).

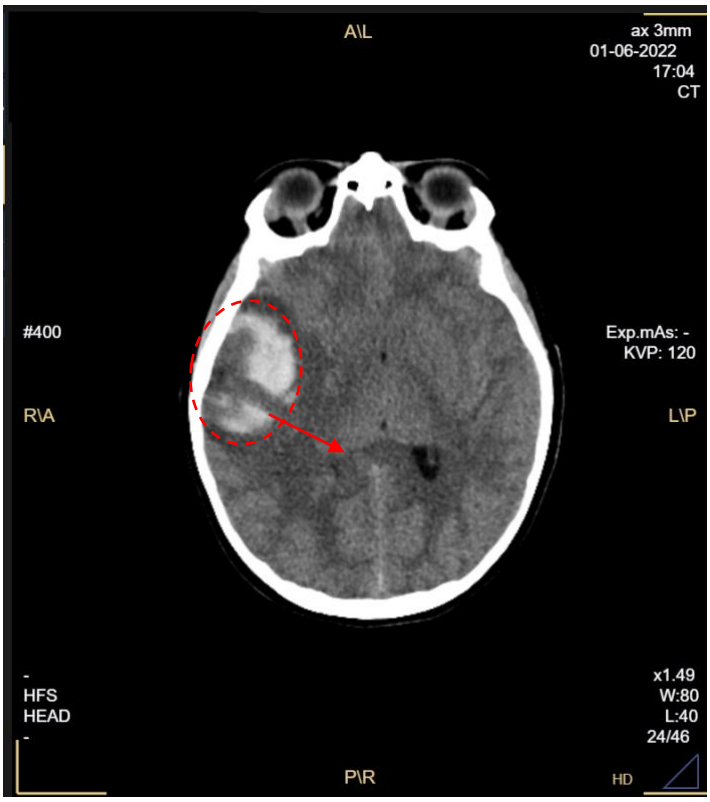


Image 6. Pre-operative CT scan showing hemorrhagic infarction in the right temporal lobe (dashed line) due to spontaneous thrombosis of the right transverse and sigmoid sinuses. The hemorrhage imposes a mass effect on the right lateral ventricle (red arrow).

She underwent initial endovascular treatment with mechanical thrombectomy and partial revascularization of the affected venous axis. However, due to persistent mass effect and radiological progression, a second endovascular procedure was performed, combining mechanical revascularization with local thrombolysis. Despite these efforts, clinical signs of raised intracranial pressure developed, including anisocoria, prompting surgical intervention.

A right-sided decompressive craniectomy was performed. Upon dural opening, the brain appeared tense and congested. Mannitol was administered intraoperatively to facilitate brain relaxation. A moderate hemispheric parenchymal bleed was noted and controlled with hemostatic agents. No significant temporal lobe hemorrhages were identified. An intraparenchymal ICP monitor was inserted in the right frontal lobe. Postoperative imaging revealed new cerebellar hemorrhage, worsening temporal edema, and ventricular dilation (*Image 7*). A control angiography revealed re-thrombosis of the right transverse sinus, which was successfully treated with further revascularization.

Image 7. Post-craniectomy CT scan showing hemorrhagic infarction with parenchymal bulging due to complete thrombosis and occlusion of the right transverse sinus.

In the following days, the patient's intracranial pressure remained stable and imaging showed regression of herniation signs. Sedation was gradually withdrawn, and she regained consciousness with residual left hemiparesis. After removal of the ICP monitor, she was weaned from mechanical ventilation and transitioned to oxygen via nasal cannula.

On transfer to the pediatric neurology ward, neurological assessment revealed a central facial nerve palsy on the left, moderate left-sided hemiparesis, and a tremor in the right hand. EEG demonstrated well-organized electrical activity, with mild asymmetry and right hemispheric slowing. MRI confirmed reduction in mass effect

and progressive normalization of ventricular size, although the sinus thrombosis persisted.

Subsequent follow-up imaging showed partial recanalization of the right transverse–sigmoid sinus. With stable platelet counts, she was deemed eligible for cranioplasty. The autologous bone flap was reimplanted, and reconstruction of the temporal region was completed using methyl methacrylate. During surgery, a small chronic subdural collection was evacuated. Postoperative recovery was initially uneventful.

Weeks later, she presented with an infected wound dehiscence at the surgical site. The autologous flap was removed due to confirmed infection with *Staphylococcus aureus*. After adequate wound management and stabilization, she underwent definitive skull reconstruction with a custom-made hydroxyapatite implant in the right frontotemporoparietal region (*Image 8*).

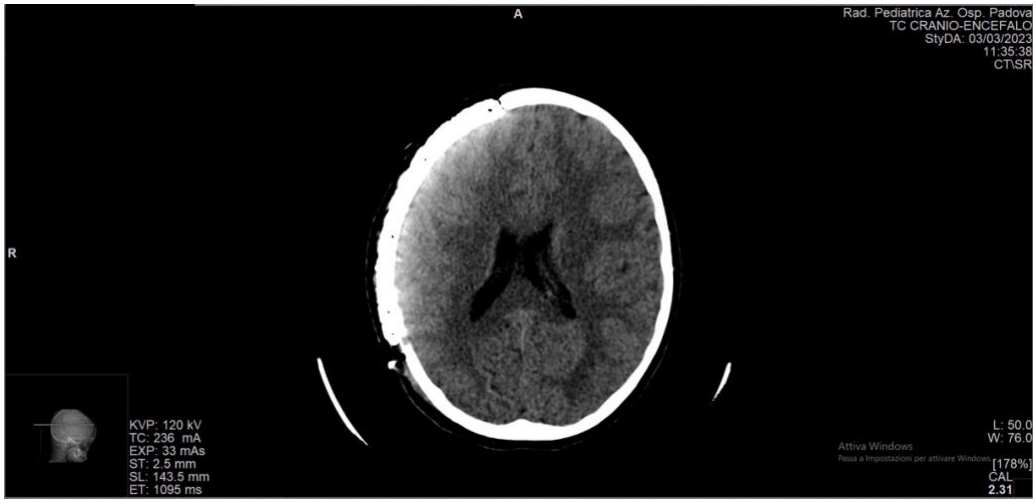
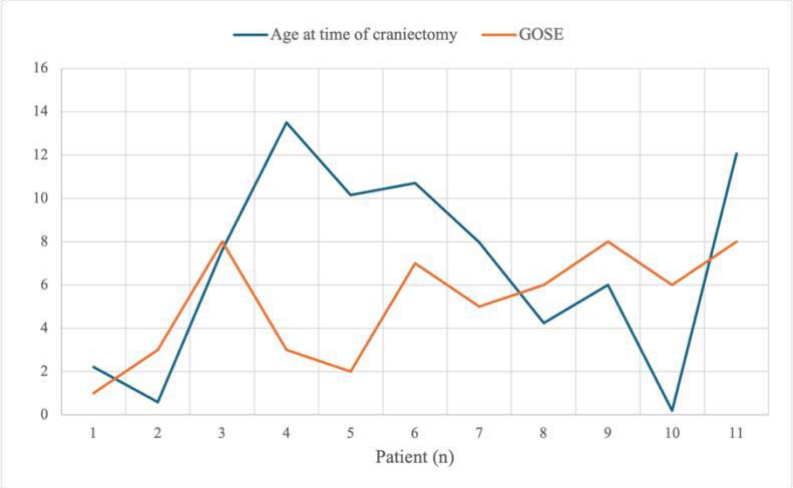


Image 8. Postoperative CT scan showing right-sided custom-made cranioplasty with hydroxyapatite implant.

4.1.3 Outcome Scores

Functional outcome at follow-up was measured using the GOS-E Peds.

Among the 11 patients, 3 patients had a poor outcome (GOSE 1–2), including one death and two vegetative states, 2 patients had severe disability (GOSE 3–4), 3 patients had moderate disability (GOSE 5-6) and the remaining 4 patients achieved a good recovery (GOSE 7–8).



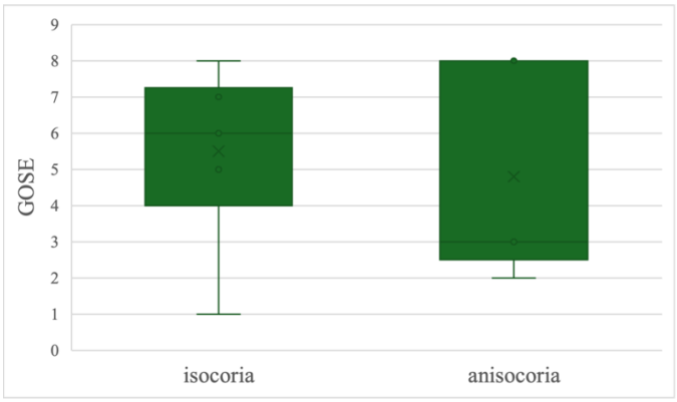
Graph 5 - Age vs GOSE trends

To explore potential age-related trends in functional recovery following decompressive craniectomy, we plotted the age at time of craniectomy of each patient against their respective GOSE score at follow-up (*Graph 5*). While no formal statistical significance was observed between age and GOSE in our previous comparative analyses, this graphical representation helps illustrate individual patient trajectories and broader distributional patterns.

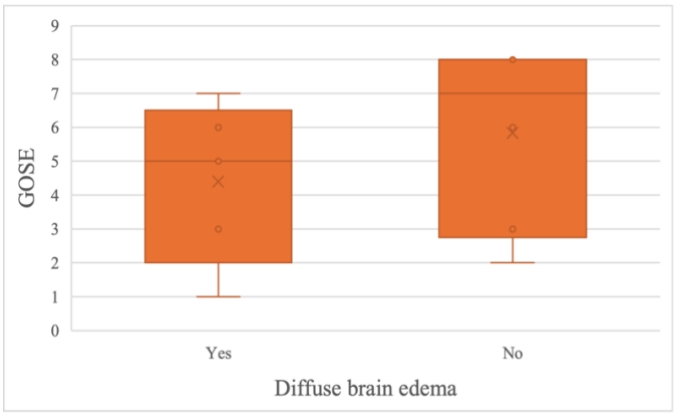
This shows considerable variability in both age and outcome, without a linear or clearly predictable relationship. Notably, some of the younger patients (e.g., Patient 1 and 2) demonstrated lower GOSE scores, while others (such as Patient 3 and 6) achieved favorable outcomes despite young age, suggesting that factors beyond age—such as injury severity, ICP control, and surgical timing—play critical roles in shaping prognosis.

Conversely, certain older patients (e.g. Patient 4 and 5) showed a mismatch between age and recovery, with lower-than-expected GOSE scores despite being in the upper age range of the cohort. On the other hand, Patient 11, the oldest in the

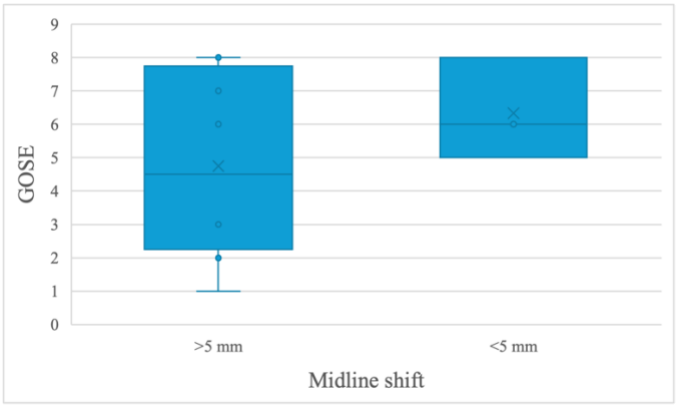
group, achieved one of the highest outcomes, suggesting age alone is not determinative.



Graph 6 - Pupillary symmetry vs GOSE



Graph 7 - Presence of diffuse brain edema vs GOSE



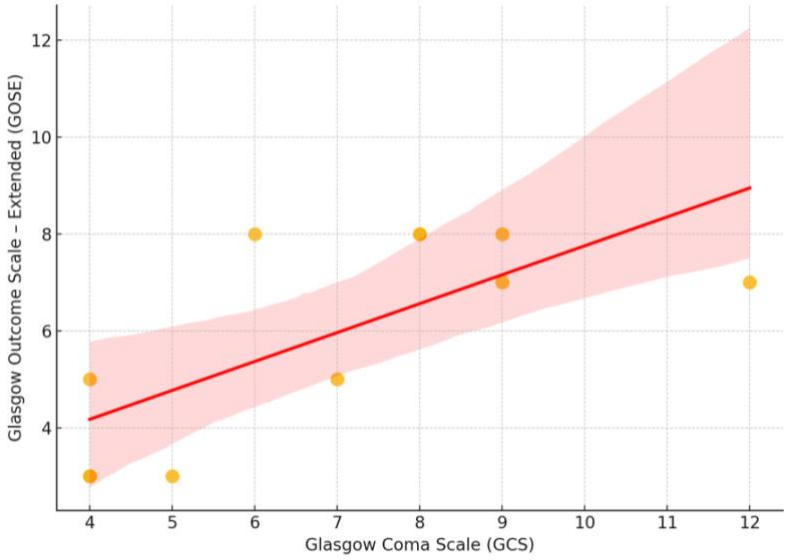
Graph 8 - Midline shift vs GOSE

The prognostic relevance of pupillary symmetry was also explored (*Graph 6*). Patients presenting with anisocoria tended to have lower GOSE scores compared to those with isocoria at admission. The median GOSE was visibly lower in the

anisocoria group, and the interquartile range suggested greater heterogeneity and a tendency toward poorer outcomes.

To evaluate the impact of diffuse brain edema on postoperative functional outcome, GOSE scores were stratified according to the presence or absence of brain edema on preoperative imaging (*Graph 7*). Patients without diffuse brain edema demonstrated a higher median GOSE compared to those with radiologically confirmed edema. The range of outcomes was broader in the edema group, with several patients showing severely impaired scores (GOSE ≤ 3), while the non-edema group exhibited a tighter distribution toward favorable scores (GOSE ≥ 6).

We further analyzed the association between midline shift on initial cranial CT and GOSE score at follow-up (*Graph 8*). Patients with midline shift > 5 mm showed a wider dispersion of GOSE scores, ranging from severe disability to good recovery. In contrast, those with < 5 mm shift exhibited less variability and generally more favorable outcomes. The median GOSE in the <5 mm group was higher, although the difference did not reach statistical significance (p=1.00).



Graph 9 - GCS vs GOSE

The Spearman correlation is used to compare GCS and GOSE being both ordinal variables: GCS is scored from 3 to 15 and although often treated as continuous, it is inherently ordinal. GOSE is explicitly ordinal (1=death, 8=upper good recovery). Moreover, Spearman's rho does not assume normal distribution or linearity of the variables.

Spearman correlation coefficient between GCS and GOSE is 0.77, with a p-value of 0.006 ($p < 0.05$). This indicates a statistically significant positive correlation: higher GCS scores at admission are associated with better long-term neurological outcomes (higher GOSE scores).

4.1.4 Comparative analysis within our Case Series

To explore potential predictors of postoperative complications in our pediatric cohort, we conducted a comparative analysis (*Table 7*) of several preoperative and intraoperative variables. These included mean age at time of craniectomy, gender, etiology of the brain injury (traumatic vs non-traumatic), type of decompressive craniectomy (primary vs secondary), presence of comorbidities, initial Glasgow Coma Scale, preoperative CT findings (midline shift and brain edema), and preoperative care setting, specifically the use of ICP monitoring devices.

For categorical variables, we applied Fisher's exact test due to the small sample size, and for continuous or ordinal variables such as GCS, we used the Mann–Whitney U test to compare distributions between groups with and without complications.

This analysis aimed to identify statistically significant trends that could inform clinical decision-making, guide risk stratification, and improve the management of pediatric patients undergoing decompressive craniectomy. While the limited sample size restricts generalizability, the findings provide important preliminary data that contribute to the evolving body of evidence on outcomes in this vulnerable.

Table 7 - Baseline data stratified by complications

Characteristics	**Any complications** (n = 6)	**No complications** (n = 5)	***p* value**
Mean age, years (SD)	5.88 ± 4.54	8.50 ± 4.83	0.412
Gender			
Male, n (%)	2 (67%)	1 (33%)	0.15
Female, n (%)	4 (50%)	4 (50%)	
Comorbidities			
Yes, n (%)	3 (50%)	3 (50%)	1.00
No, n (%)	3 (60%)	2 (40%)	
Type of DC			
Primary, n (%)	4 (50%)	4 (50%)	1.00
Secondary, n (%)	2 (67%)	1 (33%)	
Etiology			
Traumatic, n (%)	4 (57%)	3 (43%)	1.00
Non-traumatic, n (%)	2 (50%)	2 (50%)	
Median GCS (IQR)	6.5 (4.7)	5.0 (2.0)	0.78
ICP monitoring			
Yes, n (%)	5, (71%)	3, (29%)	0.5
No, n (%)	1, (33%)	2, (67%)	
Pre-operative brain CT findings			
Midline shift			
> 5 mm, n (%)	4, (50%)	4, (50%)	1.0
< 5 mm, n (%)	2, (67%)	1, (67%)	
Brain edema			
Yes, n (%)	2, (40%)	3, (60%)	0.57
No, n (%)	4, (67%)	2, (33%)	

The cohort was evenly distributed between the two groups: 6 patients (54.5%) experienced at least one postoperative complication, while 5 (45.5%) had an uneventful course. The mean age of patients who developed complications was 5.88 ± 4.54 years, compared to 8.50 ± 4.83 years in those without complications

(p=0.412), suggesting a trend toward higher complication rates in younger children, although the difference was not statistically significant.

Gender distribution did not differ significantly between groups (p=0.15), with males accounting for 67% of patients with complications and 33% of those without. Comorbidities were evenly distributed in both groups, present in 50% of cases overall (p=1.00).

Regarding surgical variables, both primary and secondary DC were evenly represented among patients with complications (50% and 67%, respectively), and no association was found between surgical timing and complications (p=1.00). Similarly, etiology (traumatic vs non-traumatic brain injury) did not influence complication rates: traumatic etiology was present in 57% of patients with complications and 43% of those without (p=1.00).

The median GCS at admission was 6.5 (IQR 4.7) in the complication group and 5.0 (IQR 2.0) in the non-complication group (p=0.78), indicating no clear relationship between initial neurological severity and surgical risk. ICP monitoring was more frequently used in patients who developed complications (71%) compared to those who did not (29%), but this difference did not reach statistical significance (p=0.50).

Pre-operative CT imaging revealed no association between the extent of midline shift and complications: both groups had 50% of patients with a shift >5 mm (p=1.00). Likewise, the presence of brain edema was not predictive of complications, occurring in 40% of patients with complications versus 60% in those without (p=0.57).

Table 8 - Effects of patients' characteristics on overall outcome

Characteristics	**Favorable outcome GOSE ≥ 6** (n = 6)	**Unfavorable outcome GOSE < 6** (n = 5)	***p* value**
Mean age at craniectomy, years (SD)	6.80 ± 4.34	6.88 ± 5.41	0.93
Gender			
Male, n (%)	1 (33%)	2 (67%)	0.24
Female, n (%)	5 (63%)	3 (37%)	
Comorbidities			
Yes, n (%)	4 (33%)	2 (67%)	0.57
No, n (%)	2 (60%)	3 (40%)	
Type of DC			
Primary, n (%)	4 (50%)	4 (50%)	1.00
Secondary, n (%)	2 (67%)	1 (33%)	(OR 0.3)
Etiology			
Traumatic, n (%)	3 (43%)	4 (57%)	0.58
Non-traumatic, n (%)	3 (75%)	1 (25%)	
Median GCS (IQR)	9 (8.0)	4.5 (2.5)	0.079
Pupillary symmetry			
Isocoria, n (%)	4 (67%)	2 (33%)	0.6
Anisocoria, n (%)	2 (40%)	3 (60%)	(OR 3.00)
ICP monitoring			
Yes, n (%)	5 (83%)	3 (17%)	0.55
No, n (%)	1 (33%)	2 (67%)	(OR 3.33)
Pre-operative brain CT findings			
Midline shift			
>5 mm, n (%)	4 (50%)	4 (50%)	1.00
<5 mm, n (%)	2 (67%)	1 (67%)	(OR 0.5)
Brain edema			
Yes, n (%)	2 (40%)	3 (60%)	0.75
No, n (%)	4 (67%)	2 (33%)	(OR 0.33)
Mean PICU stay, days (SD)	38.2 (26.79)	21.0 (9.72)	0.23
Complications			
Yes, n (%)	4 (67%)	2 (33%)	0.55
No, n (%)	2 (40%)	3 (60%)	
Mean cranioplasty timing, days (SD)	98.75 (97.75)	69.6 (66.2)	0.63

To better characterize the factors influencing postoperative outcomes in our cohort of pediatric patients undergoing DC, we conducted a focused statistical analysis comparing several clinical, radiological, and surgical variables to both the occurrence of any postoperative complications and functional outcome at follow-up, measured via the GOSE-Peds (*Table 8*). A GOSE score of 6 or above was classified as a *favorable outcome*, while scores below 6 were considered *unfavorable*.

The rationale for choosing these variables stems from prior literature suggesting their prognostic value in TBI and decompressive craniectomy, both in adult and pediatric populations. In particular, GCS at presentation, midline shift, pupillary reactivity, and the presence of diffuse cerebral edema have consistently been linked to neurological prognosis in TBI. Similarly, etiology, timing and type of craniectomy (primary vs secondary), preexisting comorbidities, and complication profile are frequently cited as influencing factors on both early surgical risk and long-term outcome. We thus selected these parameters a priori for univariate comparison.

Regarding neurological severity at admission, we observed a trend toward lower median GCS scores in the unfavorable outcome group, although this did not reach statistical significance. A Spearman correlation analysis between GCS and GOSE revealed a strong positive correlation ($\rho=0.77$, $p<0.01$), supporting its validity as a prognostic marker. Pupillary asymmetry (anisocoria) at presentation, though more frequent among those with unfavorable outcome, did not show a statistically significant association, echoing findings in other pediatric cohorts where pupil status is often less predictive than in adults due to neurodevelopmental variability.

Radiological variables, including midline shift and brain edema, were explored due to their role in surgical decision-making. While a midline shift >5 mm was more common in patients with unfavorable outcomes, this trend was not statistically significant. Similarly, the presence of cerebral edema did not correlate strongly with prognosis in our limited cohort.

The role of etiology (traumatic vs non-traumatic) was also assessed. Although patients with traumatic etiologies had a numerically lower rate of favorable outcome (4 vs 3 in the non-traumatic group), the association was not statistically significant (p=0.55). Notably, comorbidities did not appear to impact outcomes in this analysis, despite being frequent in clinical pediatric populations.

From a surgical standpoint, we compared primary vs secondary DC, ICP monitoring, and cranioplasty timing with outcome. While primary DC was more commonly associated with favorable outcomes, the result did not reach statistical significance. Interestingly, patients who underwent ICP monitoring showed a higher rate of favorable outcomes (5/8 vs 1/3), though again, not statistically significant (p=1.00, Fisher's exact). The mean timing of cranioplasty, measured in days post-DC, was slightly shorter in patients with favorable outcomes, but this difference was not statistically significant either.

The presence of any complications, including infections, hygromas, or bone flap resorption, was not statistically associated with worse outcome in this sample, though numerically more frequent in the unfavorable outcome group.

Finally, PICU stay length was compared and showed no significant difference between outcome groups, suggesting that ICU duration alone may not predict recovery trajectory.

4.2 Literature Cohort

The initial search yielded 1179 studies. After duplicates were removed and eligibility criteria applied, 139 studies were included in the final analysis, of which 68 involved only pediatric patients. Of these 8 were reviews, 14 were editorials or commentaries, 21 lacked sufficiently detailed clinical data or outcome metrics, and 23 were excluded due to date of publication, prioritizing studies published more recently to ensure alignment with current standards of care and surgical techniques.

No randomized controlled trials specific to the pediatric population were identified.

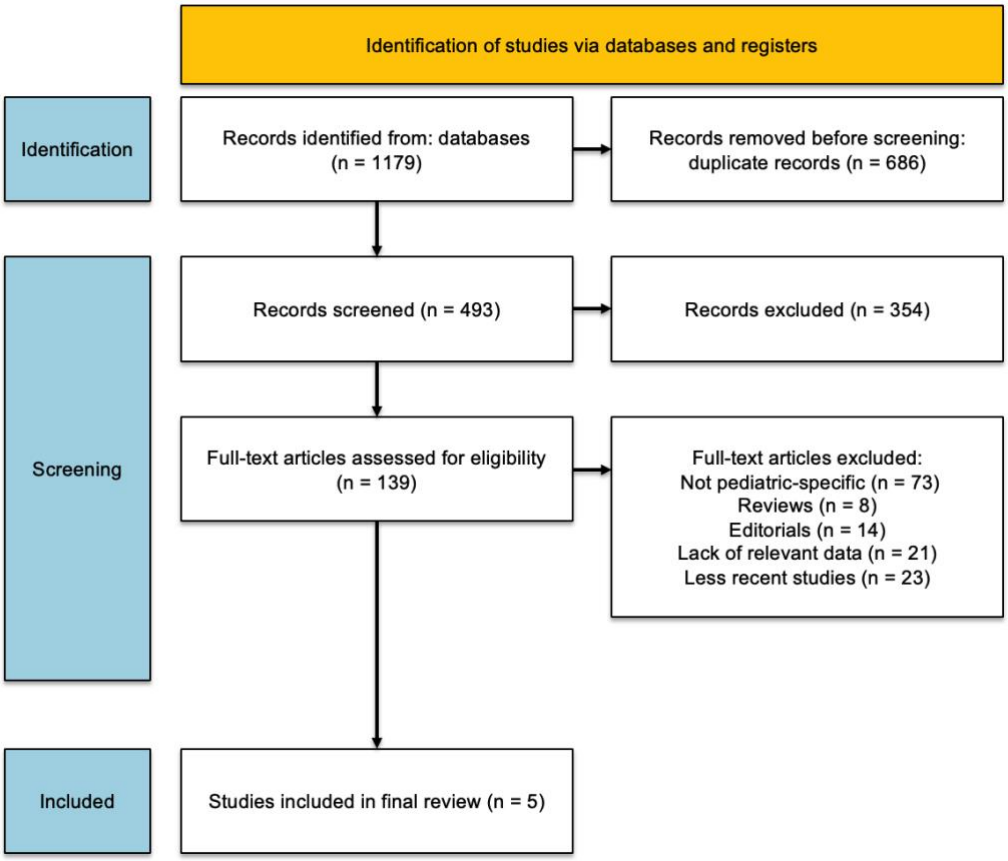


Figure 11 - PRISMA diagram used for the systematic review[72]

A total of 5 studies were included in the systematic review, encompassing over 181 pediatric patients who underwent decompressive craniectomy for traumatic or non-traumatic intracranial hypertension.

A summary of the cohorts extracted from each study is presented in *Table 7*.

Indications were consistent with those in our series: refractory ICP, radiological signs of herniation, or neurological deterioration.

The five studies included provided important, although heterogeneous, insights into the short- and long-term outcomes following DC in pediatric patients. Each study explored different etiological spectra, surgical strategies, and follow-up durations, reflecting the variability in current clinical practice.

Williams et al.[73] conducted a mixed observational study involving 30 pediatric patients (median age 6.5 months, IQR 2–50) who underwent decompressive craniectomy for non-traumatic intracranial hypertension in a tertiary pediatric ICU

between 2012 and 2017. The majority of patients were male (86.7%), and the most common etiology was intracranial hemorrhage (80%), followed by CNS infections and venous sinus thrombosis. Clinical signs at admission included altered sensorium (86.7%), seizures (83.3%), pallor (63.3%), and anisocoria (46.7%), with a median GCS of 9 (IQR 6–11). The median time from admission to surgery was 24 hours.

At hospital discharge, 53.3% of patients had a good outcome (GOS-E Peds 5-8), while 46.7% had poor outcomes (GOS-E Peds 1-4), including eight deaths (26.7%), two of which occurred during the PICU stay and six during follow-up (up to 6 months). Neurological sequelae among survivors at discharge included seizures in 89.2% and hemiparesis in 57.1%. At a median follow-up of 12 months, 21 children were evaluated: 48.2% maintained a favorable long-term neurological outcome, while 51.8% had a poor outcome (including those who had died). Persistent neurological deficits included hemiparesis (47.6%), seizures (33%), visual deficits (19%), and dystonia (14%). Only 3 patients (14.3%) underwent successful bone flap reimplantation without complications.

On univariate analysis, anisocoria and focal neurological deficits at admission were associated with poor outcome, but anisocoria remained the only independent predictor on multivariate regression (OR 7.33; 95% CI 1.38–38.87; p=0.019). No variable significantly predicted mortality. The study highlights the potential utility of DC in non-traumatic pediatric ICH, especially in the presence of focal lesions and midline shift, though outcomes remain variable and long-term sequelae common.

In a retrospective analysis Taşkapılıoğlu et al.[74] studied 11 pediatric patients undergoing DC for acute subdural hematoma, aiming to assess early surgical intervention outcomes in this context. The study cohort included children aged between 8 months and 15 years (median age: 48 months), with a near-equal gender distribution (45.5% male). The etiologies of injury were falls (n=4), traffic accidents (n=5), and blunt trauma from a direct hit (n=1).

The mean GCS score at admission was 7.8, with 54.5% of patients presenting with GCS≤8. Only one patient (9.1%) had anisocoria on admission. All patients underwent DC with duraplasty within a median of 4 hours post-injury (range: 1-7

hours), regardless of GCS severity. The decompression area measured a median of 325 cm^2 (range: 157.5-792 cm^2), with 7 unilateral and 4 bilateral DCs performed.

All patients were admitted postoperatively to the pediatric ICU, with a median PICU stay of 10 days and an average hospitalization duration of 22 days. Cranioplasty was performed at a median of 4.5 months after DC (range: 1-12 months). Notably, the mean follow-up period was 3.7 years, allowing for meaningful assessment of long-term neurological outcomes.

At discharge, the modified Rankin Scale (mRS) scores ranged from 1 to 4 (median mRS=3), while at follow-up the median mRS improved to 1.6, indicating substantial neurological recovery over time. No perioperative deaths were reported in the cohort. The functional outcome was generally favorable, although the authors caution that small sample size limits broad generalizability.

Regarding postoperative complications, the study reported a high rate of bone flap resorption, with 7 patients (63%) experiencing aseptic resorption, and 3 requiring reoperation and additional cranioplasty. Infectious complications were also observed: 2 cases of meningitis and 2 wound infections. Seizures were a frequent postoperative finding but not further quantified.

The authors conducted correlation analyses between mRS scores and clinical/surgical variables, including age, preoperative GCS, time to decompression, decompression area, and cranioplasty timing, using Spearman's correlation. However, specific correlation coefficients and statistical significances were not provided in the summary. Nevertheless, the study advocates for early DC (within 2 hours of trauma) regardless of initial GCS, proposing that early decompression may mitigate secondary injury and improve long-term functional recovery.

In conclusion, early DC with duraplasty was shown to be a safe and potentially beneficial intervention for pediatric SDH, with encouraging long-term functional outcomes and zero mortality, though bone flap complications remain a significant concern, especially in growing children.

Semenova et al.[75] present one of the most comprehensive retrospective cohorts on pediatric DC for refractory intracranial hypertension, involving 64 children with severe TBI who underwent secondary DC over a 6-month period. These cases were selected from a broader population of 287 pediatric TBI patients, of whom 169

received ICP monitoring in accordance with contemporary severe TBI protocols. The study applied rigorous radiological and clinical criteria for surgical indication, including brainstem displacement or threatened herniation and progressive obliteration of basal cisterns on CT imaging. Frontotemporoparietal DC was performed in patients with lateral displacement (n=34), while bifrontal DC was chosen in cases of axial dislocation (n=30).

The mean age was 10.8 ± 4.8 years, and 58% of patients had polytrauma, reflected by a mean Injury Severity Score of 28.3 ± 10.2. Etiologically, traffic accidents were the predominant cause (70%), followed by falls (18%), violence (8%), and miscellaneous causes (4%). Most patients (n=46) were transferred from peripheral hospitals, often after a delay; only 18 were directly admitted from the injury site. The cohort was stratified based on timing of admission, with 49 patients arriving within 24 hours and 14 later, a variable that influenced both clinical presentation and prognosis.

The mean GCS score at admission was 6 ± 2, and ICP monitoring was conducted in 87.5% (n=56) of patients. In the remaining eight, urgent DC was performed due to herniation syndrome. Neuromonitoring included the E2 parameter, a derived measure combining the squared mean and dispersion of ICP values to quantify ICP dynamics. Most patients had a Marshall CT classification of 3 at baseline. CT was repeated in cases of clinical deterioration or sustained ICP > 20 mmHg and served to guide surgical decision-making through multidisciplinary consensus.

Outcomes were assessed at 6 months post-injury using the GOS. Overall, 45.3% achieved a good recovery (GOS 4-5), 31% had severe disability (GOS 3), and 23.4% experienced poor outcomes or died (GOS 1-2). Among the survivors, early cranioplasty was performed between 30-55 days post-DC. 8 children (12.5%) required ventriculoperitoneal shunting for post-traumatic hydrocephalus.

Using binary logistic regression, the study identified key predictors of unfavorable outcomes: lower GCS, ICP > 40 mmHg, combined trauma, dilated and unreactive pupils, and midline shift > 5 mm. Interestingly, the presence of ICP monitoring, the number of ICP spikes, and even Marshall score alone were not independently predictive of outcome. Pupillary status and ICP dynamics, particularly the E2 index, were found to be most strongly associated with prognosis. ROC analysis confirmed that GCS and ICP held the highest predictive value (AUC), reinforcing their clinical utility.

The authors concluded that while DC can be a lifesaving intervention, outcomes remain highly dependent on early admission, severity of initial brain insult, and neuromonitoring parameters. Moreover, the prompt reconstruction of the skull defect may reduce complications such as hydrocephalus or external cerebral herniation, further supporting protocolized post-DC management in pediatric severe TBI.

Hubertus et al.[76] conducted a retrospective cohort study examining the clinical characteristics, management, and outcomes of 48 pediatric patients (≤16 years) with severe traumatic brain injury, defined as a GCS≤8, admitted to a tertiary pediatric intensive care unit between 2008 and 2018. The study also compared these patients with a historical cohort of 53 children managed between 1996 and 2007 at the same institution. The median age at admission was 4 years, and 58% were male. The leading causes of trauma were falls from height (52%) and traffic accidents (44%), with a significant age difference between mechanisms (falls median age 4 years; traffic accidents median age 6 years; p=0.0071). The median GCS at presentation was 3, and most patients (86%) required intubation. Neurological examination revealed anisocoria in 31% and impaired pupillary response in 42%.

Radiologically, skull fractures were present in 73%, and intraventricular hemorrhage in 21%. The most common intracranial lesions were contusions (48%), subdural hematomas (33%), epidural hematomas (8%), diffuse edema (8%), and intracerebral hematomas (2%). Midline shift was observed in 56% of cases, with a median deviation of 2 mm.

In terms of treatment, 29 children (60%) were managed conservatively, while 8 (17%) underwent craniotomy with direct reimplantation of the bone flap, and 11 patients (23%) received DC with duraplasty. ICP monitoring was employed in the vast majority (85%) via external ventricular drain and in 38% with intraparenchymal probes, with some overlap (25%). The median time from admission to surgery was 1 day (range 0–6), while median ventilation time was 8 days, ICU stay 15 days, and total hospitalization 24 days. In-hospital mortality was 15% (7 patients), with three patients dying within the first 24 hours post-admission.

When comparing the recent cohort to the historical one, although the recent patients were generally younger and had lower GCS at presentation, the overall mortality and clinical outcomes were similar. Outcome assessment using the

Glasgow Outcome Scale at 3, 12, and 36 months demonstrated comparable and often favorable recovery trajectories in both cohorts. The study highlights the benefits of evolving intensive care protocols, such as more widespread use of EVD and early surgical intervention. While no statistical superiority was shown for DC in terms of long-term outcome, the authors emphasize the importance of consistent and aggressive therapy in optimizing survival and functional recovery in pediatric severe TBI.

Korhonen et al.[77] conducted a retrospective cohort study encompassing all pediatric patients who underwent DC for intractable intracranial hypertension at the Oulu University Hospital in Northern Finland over an 11-year period (2009–2019). The study included 24 children (median age: 16.0 years), with TBI being the most common indication (83%), followed by ischemic stroke (8%), encephalitis (4%), and spontaneous hemorrhage (4%). The median preoperative Glasgow Coma Scale (GCS) was 5.0.

Of the 24 patients, 6 (25%) underwent primary DC immediately after the primary insult, while 18 (75%) had secondary DC due to refractory intracranial pressure (ICP). The mean time to surgery was 1.6 days from injury. The majority of procedures consisted of frontotemporoparietal hemicraniectomy (50%), followed by bifrontal (two-flap, 21%; one-flap, 25%) and one bilateral hemicraniectomy (4%). The average bone flap size was 103 cm^2. Only 7 patients had reliable preoperative ICP data, all of which exceeded 25 mmHg.

The mortality rate was 12.5% (3/24), with all deaths occurring within 24 hours of surgery. Among survivors (n=21), 63% (15 patients) achieved a favorable long-term neurological recovery, defined as GOSE≥7. Furthermore, 86% of survivors returned to school, underscoring meaningful functional outcomes even after severe injury. Notably, hydrocephalus requiring shunting was associated with poor recovery and failure to return to school ($p=0.01$ and $p=0.03$, respectively). Absent basal cisterns on initial CT were significantly associated with mortality but not with poor functional recovery among survivors.

Postoperative complications occurred in 52% of survivors, with 19% requiring surgical intervention. Complications included subcutaneous CSF collections, surgical site infections (SSI), and symptomatic intracerebral hematomas. Regarding cranioplasty, performed at a mean of 3.5 months after DC, 60% received autologous

bone flaps (with a mean Oulu Resorption Score of 5.1), while the remainder received patient-specific implants. Cranioplasty-related complications were observed in 25% of cases, and re-cranioplasty was required in 20%.

Overall, the study highlights that, even in children with severe radiological and clinical presentation, DC may result in favorable neurological and functional outcomes. Importantly, long-term morbidity was influenced more by postoperative complications such as hydrocephalus than by initial injury severity metrics such as GCS or pupillary status. The findings support DC as a potentially effective intervention for selected pediatric patients, provided that robust follow-up and rehabilitative support are ensured.

Table 7 - Comparative table: our Institutional Case Series vs Literature Case Series

STUDY	N.	MEDIAN AGE (YEARS)	ETIOLOGY	PRIMARY/ SECONDARY DC	MEAN GCS AT ADMISSION	ANISOCORIA (%)	MIDLINE SHIFT >5MM (%)	ICP MONITORING	COMPLICATION RATE (%)	MORTALITY (%)
WILLIAMS ET AL.	30	0.54	100% non-traumatic	All secondary	9	46.7	Common, not quantified	Not specified	93	26.7
TAŞKAPILIOĞLU ET AL.	11	4.0	100% traumatic (SDH)	11 primary	7.8	9.1	Not specified	All patients	63	0
SEMENOVA ET AL.	64	10.8	100% traumatic	64 secondary	6.0	Not specified	Associated with poor outcome	87.5% monitored	12.5	23.4
HUBERTUS ET AL.	48	4.0	100% traumatic	23% DC (11 patients), unspecified	3.0	31	56	85%	36	15
KORHONEN ET AL.	24	16.0	83% traumatic 17% non-traumatic	6 primary 18 secondary	5.0	Not associated with outcome	Associated with mortality	29.2% (7/24) with reliable ICP data	52	12.5
OUR CASE SERIES	11	7.6	55.6 % traumatic, 44.4% non-traumatic	8 primary 3 secondary	7.1	63.6	70	54.5% monitored	54.5	9.1

4.3 Comparative analysis of long-term Outcomes

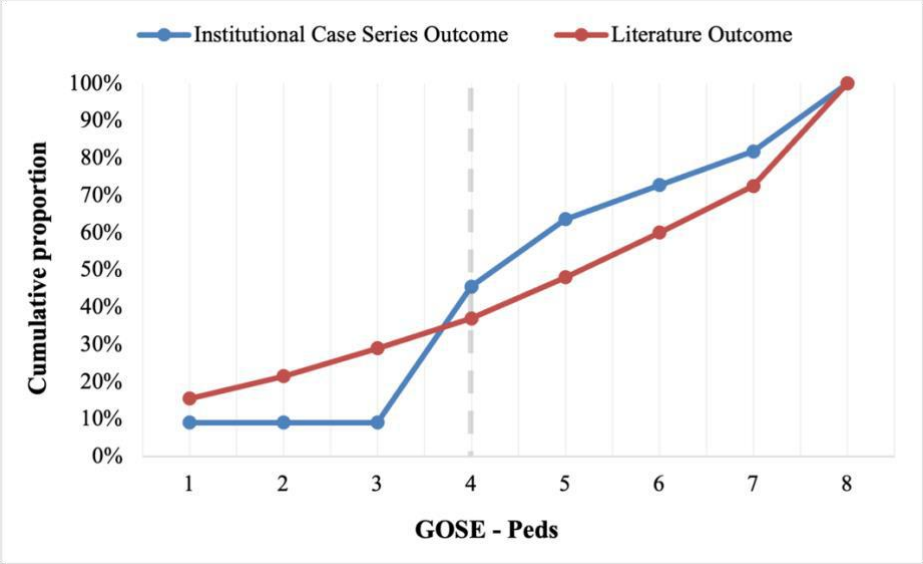
To facilitate a standardized comparison of long-term outcomes following decompressive craniectomy in pediatric patients, we selected the Extended Glasgow Outcome Scale (GOSE) as a common reference framework. This scale is widely adopted in neurotrauma research due to its ability to capture both functional and cognitive recovery across an 8-point continuum, ranging from death (GOSE=1) to upper good recovery (GOSE=8).

Each of the selected studies reported outcomes using different scoring systems, requiring harmonization before cumulative comparison. Our own case series utilized the GOSE directly, allowing for immediate inclusion. In contrast, *Taşkapılıoğlu et al.* employed the modified Rankin Scale (mRS), defining favorable outcomes as mRS ≤ 2. Based on established equivalences in the literature, this was mapped to GOSE scores of 6–8, as mRS ≤ 2 has been shown to correlate with moderate to good recovery on the GOSE scale.[78] *Semenova et al.* reported outcomes using the original Glasgow Outcome Scale (GOS), with favorable outcomes defined as GOS 4–5. This was also mapped to GOSE scores of 6–8, in line with validated crosswalks between the two scales.[79]

Williams et al. only reported the proportion of patients achieving a favorable outcome, without specifying the functional scale used. Therefore, we inferred a plausible cumulative distribution from the reported endpoint, interpolating intermediate values based on the assumption of typical distributional patterns observed in pediatric cohorts with severe brain injury, as documented in prior clinical studies.[80] *Hubertus et al.* did not provide explicit outcome stratification; for this reason, a hypothetical progression was constructed for comparative purposes. This estimation was based on the reported mortality rate (15%) and the general trend of outcomes observed in similar pediatric cohorts.[67] However, the absence of granular data introduces important limitations: the internal distribution of survivors across disability levels (GOSE 2–8) remains unknown, and the inferred trajectory may not reflect the actual functional outcomes of the cohort. Therefore, this approximation must be interpreted with caution and is presented solely to maintain visual continuity in the cumulative comparison graph.

For *Korhonen et al. (2022)*, the reported mortality rate was 12.5% (3/24), with all deaths occurring within 24 hours post-surgery. Among survivors (n=21), 63% (15 patients) achieved a favorable long-term neurological outcome, defined as GOSE ≥ 7, and 86% returned to school. To integrate this data into the cumulative GOSE framework, we assigned the mortality group to GOSE 1 (12.5%) and the favorable group to GOSE 7–8 (62.5%). The remaining six patients were conservatively distributed across scores 3–6 to reflect moderate to severe disability, and cumulative percentages were derived accordingly.

Based on these mappings, we calculated the cumulative proportion of patients at or below each GOSE score (1 to 8) for each study. The resulting data allowed us to construct a cumulative line graph in which each line represents the progressive proportion of patients across GOSE levels. This graphical method enables direct visual comparison of recovery profiles.



Graph 10 - Cumulative distribution of long-term outcomes following DC in pediatric patients, expressed using a harmonized GOSE-like ordinal scale (1=death; 8=upper good recovery).

The final graph compares the cumulative distribution of GOSE scores in our case series (n=11) with the averaged distribution derived from the five selected studies (*Williams et al.*, *Taşkapılıoğlu et al.*, *Semenova et al.*, *Hubertus et al.*, and *Korhonen et al.*). A vertical threshold line at GOSE=4 is included to indicate the demarcation

between unfavorable (GOSE ≤ 4) and favorable outcomes (GOSE ≥ 5). This approach offers a structured and transparent method for synthesizing heterogeneous outcome measures into a unified framework, enabling cross-study comparisons.

5 DISCUSSION

5.1 Interpretation of Results

The analysis of our institutional case series highlights the complex and multifactorial nature of outcomes following decompressive craniectomy in the pediatric population. Although the limit in size of the cohort and the heterogeneity in both etiology and clinical presentation, it offered a valuable opportunity to investigate both functional outcomes and complications using a structured statistical approach.

Our analysis of the clinical evolution after surgery aimed to elucidate potential predictors of increased surgical morbidity. While younger age appeared to be associated with a higher incidence of complications (mean 5.88 vs 8.50 years), this trend did not reach statistical significance (p=0.412). However, the observed trend may be clinically meaningful, as younger children likely have greater physiological vulnerability, including immature cerebral autoregulation and increased susceptibility to infections, all of which may predispose them to a more complicated postoperative course.

A similar absence of significance was noted for sex, etiology, and type of DC, suggesting that no single demographic or surgical factor clearly delineated risk for complications. Nonetheless, the overrepresentation of males in the complication group (67%) may reflect the generally higher prevalence of TBI in boys, rather than a direct biological effect. This may be due in part to the heterogeneity of the cohort and the relatively high baseline vulnerability of all patients undergoing DC, regardless of clinical context.

Interestingly, comorbidities, often assumed to predispose to worse perioperative outcomes, did not correlate with complication rates (p=1.00), perhaps reflecting the predominant role of acute neurologic and hemodynamic instability in early postoperative morbidity. Similarly, ICP monitoring, though more frequent in patients who developed complications (71% vs 29%), was not statistically predictive (p=0.50). This may reflect a selection bias, where patients deemed at higher baseline risk were more likely to undergo intensive monitoring, rather than the monitoring itself causing complications. Still, the potential for procedural risks

(e.g., infection, hemorrhage) associated with invasive monitoring warrants further study.

Radiological parameters such as midline shift and brain edema also failed to show significant predictive value in this context. This finding highlights the limit of using isolated imaging markers to predict surgical morbidity, especially in a pediatric population where radiological signs may not correlate linearly with clinical deterioration. Nonetheless, the pathophysiological plausibility remains significant midline shift and edema contribute to raised ICP and ischemic damage, particularly in children. Thus, even without statistical confirmation, these findings retain clinical importance.

In parallel, we examined predictors of long-term functional outcome, measured via the GOS-E Peds, with a threshold of ≥ 6 defining favorable recovery. This comparison included a partially overlapping set of variables, enriched by outcome-focused indicators such as cranioplasty timing, complication status, and PICU duration. The association between younger age and outcome remains ambiguous. While some younger patients showed poor results, others recovered well, and no statistically significant correlation was observed between age and GOSE. This variability may reflect the complex balance between neuroplasticity and vulnerability in developing brains: younger patients may have greater potential for recovery but are also more susceptible to diffuse injury and long-term developmental consequences.

The initial GCS score was strongly associated with outcome, as confirmed by Spearman correlation ($\rho=0.77$, $p < 0.01$), reaffirming its central role as a prognostic tool in pediatric TBI and neurocritical care. While the median GCS was numerically lower in the unfavorable outcome group, this difference did not reach significance in non-parametric testing, likely due to the limited sample power.

Pupillary asymmetry (anisocoria), often considered a marker of brain herniation, was more frequent in patients with poor outcome, yet statistical significance was not achieved. Although not statistically significant due to sample size constraints, the median GOSE score was lower in patients with anisocoria, and the distribution of outcomes suggested a higher likelihood of severe disability or mortality in this subgroup. This trend echoes findings from large traumatic brain injury cohorts,

where pupillary response has been strongly associated with herniation syndromes and brainstem involvement.[81]

Radiological markers demonstrated non-significant trends (Fisher's p=1.00): patients with midline shift >5 mm and evidence of cerebral edema were more likely to have unfavorable outcomes, but with wide variability. These findings suggest that structural displacement or diffuse swelling alone may be insufficient to predict prognosis, particularly without integrating dynamic parameters such as ICP trends or CPP metrics. However, this finding is pathophysiologically coherent, as cerebral edema and midline displacement contribute to elevated intracranial pressure and subsequent ischemic damage, particularly in the immature pediatric brain. Thus, although the difference in outcome did not reach statistical significance, the pattern warrants attention and supports early aggressive management of cerebral swelling.

The role of ICP monitoring remains debated in pediatric populations. In our series, a higher proportion of patients with ICP monitoring achieved favorable outcomes (5 out of 7), compared to those without monitoring (1 out of 4), although the small sample precluded significance. These findings tentatively support the utility of ICP-directed therapy, consistent with Brain Trauma Foundation guidelines[37], particularly when integrated into standardized protocols.

With respect to etiology, non-traumatic brain injuries were slightly more likely to be associated with favorable outcomes, but no statistically significant relationship emerged (p=0.55). This reinforces the growing evidence that non-traumatic etiologies may not necessarily confer a worse prognosis, a hypothesis supported by modern series describing favorable recoveries following DC for encephalitis, CVST, and spontaneous hematomas.[82,83]

Interestingly, primary versus secondary DC did not appear to strongly influence outcomes, though patients receiving primary DC showed numerically better recovery rates. The small number of secondary DC cases, and their likely greater baseline severity, may confound interpretation. Rather, it may be the interplay between timing, ICP dynamics, lesion progression, and therapeutic escalation that ultimately modulates outcome. This hypothesis supports the goal of creating individualized treatment trajectories.

Similarly, shorter cranioplasty intervals and the presence or absence of complications did not significantly influence GOSE scores, although trends suggested that earlier reconstruction and absence of postoperative morbidity could be linked to better functional trajectories.

Notably, the duration of PICU stay was not associated with outcome. This finding suggests that intensive care burden may reflect acute illness severity more than long-term neurologic recovery, highlighting the importance of separating survival and morbidity endpoints in pediatric neurosurgical outcomes research.

These findings illustrate that no single variable alone (demographic, clinical, radiological, or surgical) sufficiently explains the wide range of functional outcomes observed following pediatric DC. Instead, the interaction of multiple dynamic factors, including timely intervention, adequate ICP control, and post-acute rehabilitation, likely determines recovery. This reinforces the value of integrated care pathways and multimodal monitoring in pediatric neurocritical care.

While many individual variables did not reach statistical significance, likely due to sample limitations, the trends observed are consistent with prior reports and suggest that initial GCS, pupillary status, midline shift, and cerebral edema are all clinically relevant factors that should inform early decision-making.

5.2 Comparison with Literature

When comparing our case series with the five selected studies—Williams et al., Taşkapılıoğlu et al., Semenova et al., Hubertus et al., and Korhonen et al.—several similarities and distinctions emerge regarding patient characteristics, treatment modalities, complications, and outcomes.

5.2.1 Age and Etiology

Our cohort had a median age of 7.6 years (mean 6.8 ± 4), aligning with Taşkapılıoğlu et al. (median 4 years) and Semenova et al. (mean 10.8 ± 4.8). In contrast, Williams et al. included significantly younger patients (median 6.5 months), focusing exclusively on non-traumatic etiologies, while Korhonen et al. reported an older population (median 16 years). This variability underscores the heterogeneous age distribution typical in pediatric DC series, influenced by local referral patterns and surgical indications. The relative homogeneity of age in our cohort, positioned between infant and adolescent extremes, may have favored a more stable perioperative course, as younger infants are known to exhibit greater physiological fragility, and older adolescents may present with more complex comorbidities or secondary insults.

Regarding etiology, our distribution (55.6% traumatic vs 44.4% non-traumatic) reflects a broader spectrum than most comparative studies. While Semenova, Hubertus, and Korhonen focused mainly on traumatic brain injury, and Williams investigated exclusively non-traumatic cases, our inclusion of conditions such as encephalitis and CVST, often associated with better prognoses[82,83], may have contributed to the relatively favorable outcomes observed.

5.2.2 Initial Neurological Status and Radiology

The mean GCS in our cohort was 7.1 ± 4, comparable to Taşkapılıoğlu (7.8) and Semenova (6 ± 2), slightly higher than Hubertus (median 3), and lower than Williams (median 9), the latter consistent with its non-traumatic focus.

Pupillary asymmetry (anisocoria) was noted in 63.6% of our patients, higher than Hubertus (31%) and similar to Williams (46.7%), where it was the sole independent predictor of poor outcome. Despite the relatively high rate of anisocoria, our cohort achieved a comparable or better functional recovery, which

may reflect earlier recognition and aggressive intervention protocols, mitigating herniation-related damage.

Midline shift >5 mm was found in 70% of cases, paralleling Semenova and Hubertus, and brain edema in 72%, consistent with most studies. While these findings did not predict outcome statistically, their pathophysiological relevance remains, supporting the need for early and aggressive ICP management.

5.2.3 Timing and Type of Decompressive Craniectomy

Primary DC predominated in our cohort (72.7%), similar to Taşkapılıoğlu and Korhonen. In contrast, Semenova and Williams exclusively reported secondary DC, while Hubertus presented mixed timing. The potential benefit of primary DC, allowing earlier ICP control, was not statistically confirmed in our cohort (OR=0.75, p=1.00), consistent with Hubertus and Korhonen. Nevertheless, our data support the emerging pediatric neurocritical care paradigm favoring early decompression in selected cases.

5.2.4 Postoperative Complications

Complications occurred in 54.5% of our patients, mirroring Korhonen (52%) and slightly lower than Taşkapılıoğlu (63% flap resorption rate). These included CSF leaks, encephalic herniation, and hygromas, which are consistent across the literature.

Despite this relatively high complication rate, our favorable functional outcomes suggest that structured monitoring, early detection, and robust management protocols may mitigate their clinical impact. Notably, no demographic variable, such as age, which trended younger in the complication group (mean 5.88 vs 8.50, p=0.412), or clinical variable (age, GCS, comorbidities, ICP monitoring, midline shift, or edema), significantly predicted complication risk, paralleling findings by Hubertus and Korhonen. This underscores the multifactorial nature of surgical risk.

5.2.5 Functional Outcomes (GOSE-Peds)

A total of 63.6% of our cohort achieved favorable outcomes (GOSE ≥ 6), like Korhonen (63%) and higher than Williams (48.2%). Semenova reported 45.3% achieving GOS 4–5, using a slightly different threshold. Taşkapılıoğlu described

excellent recovery (mRS median 1.6), but small sample size and use of a different scale limit direct comparability.

Our GCS was significantly correlated with GOSE (ρ=0.77, p=0.006), in line with Semenova's logistic regression and ROC findings. Other variables (e.g. edema, anisocoria, midline shift, comorbidities) showed no significant association with outcome, echoing the results from Korhonen. This reinforces the primacy of GCS as a reliable early prognostic indicator.

Interestingly, our cohort showed no significant outcome differences emerged based on etiology (traumatic vs non-traumatic, p=0.55) or complication status (p=1.00), challenging common assumptions that these are dominant prognostic drivers. This aligns with the nuanced findings in Korhonen, where neither GCS nor pupillary response was a strong outcome predictor among survivors.

5.2.6 Cranioplasty Timing and Protocols

Our median cranioplasty interval (81 days) falls between Semenova (30–55 days) and Korhonen (3.5 months). No significant association was found between cranioplasty timing or flap type and outcome, consistent with findings by Taşkapılıoğlu and Korhonen.

However, earlier cranioplasty may support cerebral hemodynamics and reduce late complications. Our streamlined perioperative and rehabilitation protocols may have contributed to more consistent recovery, despite the lack of statistical correlation.

5.3 Cumulative GOSE-Based Outcome Comparison

5.3.1 Mortality Rates (GOSE 1)

In our series, mortality (GOSE = 1) occurred in 9.1% of cases. This is 6.4 percentage points lower than the average mortality reported across the five selected studies (15.5%). While this numerical difference may suggest a benefit related to earlier decompression or center-specific practices, caution is warranted in interpretation given the small sample size and the likely variability in baseline severity and inclusion criteria.

5.3.2 Unfavorable vs Favorable Outcomes (GOSE ≤ 4 vs ≥ 5)

Using a threshold of GOSE ≤ 4 to define unfavorable outcomes, 45.5% of our cohort fell into this category, compared to an average of 54% in the pooled literature. This represents an 8.5% improvement in outcome distribution toward the favorable end of the spectrum. While modest, this shift may reflect improvements in perioperative care, standardized ICP management protocols, and the early initiation of neurorehabilitation programs, all elements emphasized in our institutional workflow.

5.3.3 Higher Recovery Tiers (GOSE ≥ 7 and GOSE = 8)

A particularly notable finding was that 81.8% of patients in our cohort achieved at least GOSE 7, defined as "lower good recovery." This compares favorably with the average 72.5% reported across the comparative studies, indicating a +9.3% advantage. This suggests that our patients were more likely to return to a functional, socially integrated state of recovery.

However, at the very top of the recovery spectrum (GOSE = 8, “upper good recovery”), 36.4% of our patients reached this level—identical to the cumulative literature average. This convergence suggests a ceiling effect common to both our institution and other centers, possibly reflecting intrinsic limitations in complete neurological recovery following severe brain injury in childhood.

5.3.4 Methodological Considerations

It is essential to interpret these results in light of methodological limitations. Differences in outcome scales (e.g., use of GOS vs GOSE-Peds), timing of outcome assessment, and patient selection criteria may account for some of the observed differences. Although we applied a harmonized GOSE-based framework to ensure comparability, the translation of functional outcomes across scales introduces some degree of approximation.

Nonetheless, this harmonization provides a valuable reference point to assess relative outcome quality across studies and suggests that our center's multidisciplinary model of care may yield outcomes at least as favorable, and potentially superior, in specific recovery domains.

5.3.5 Clinical Implications

Collectively, these outcome comparisons reinforce the hypothesis that certain institutional practices may synergistically support improved long-term recovery. These include:

- A higher rate of primary DC,
- Standardized ICP monitoring and early surgical intervention,
- Integrated post-acute rehabilitation, and
- Streamlined timing of cranioplasty.

While none of these factors alone reached statistical significance in our internal analysis, their combined effect may explain the improved distribution of outcomes, particularly in the intermediate and higher GOSE ranges. Future multicentric analyses with larger cohorts are needed to clarify the independent contribution of these variables.

5.4 General Considerations and Implications

The comparative and statistical analyses presented in this study highlight several clinically relevant insights regarding DC in pediatric patients. Foremost among these is the confirmation that functional recovery is shaped by the interaction of multiple dynamic variables, rather than by any single clinical or radiological marker. This complexity underscores the limitations of traditional univariate risk stratification and supports a paradigm shift toward individualized, multimodal care pathways.

In clinical practice, the absence of strong, statistically significant predictors for postoperative complications or poor outcomes, even in the presence of classic warning signs such as anisocoria or midline shift, suggests that decisions regarding surgical timing, monitoring, and escalation of care should not rely on isolated indicators. Instead, they should reflect the evolving clinical context. The trends observed in our series, including the apparent benefit of ICP monitoring and the non-inferiority of non-traumatic etiologies—are aligned with contemporary neurocritical care literature, which increasingly favors contextualized, protocol-driven management over static prognostic models.[37,54,77]

The GOSE-based cumulative comparison further refines these observations by situating our outcomes within the broader landscape of published data. While numerically favorable, our results mirror a consistent trend across studies: a distributional plateau in which a substantial proportion of survivors fail to achieve full functional recovery. This reflects a key clinical reality, **survival is no longer the central challenge in pediatric neurotrauma; quality of survival is**. Achieving upper-tier functional outcomes remains elusive and likely depends on variables beyond the acute care phase, including access to specialized neurorehabilitation, socioeconomic status, and family support systems.[84]

These findings have critical implications for post-discharge planning. The limitations of the GOSE-Peds in capturing nuanced neurocognitive and psychosocial sequelae, especially in younger children, highlight the need for long-term outcome assessments to incorporate multidimensional tools. These may include pediatric quality of life measures and standardized neuropsychological evaluations, which can provide insights into school reintegration potential, behavioral and emotional regulation, and caregiver burden. Such domains are central to recovery yet poorly reflected by functional outcome scales alone.[85]

Several methodological limitations must be acknowledged. The relatively small sample size limits the statistical power of our analyses, and the retrospective design introduces a risk of selection and information bias. Furthermore, the comparative component, although carefully harmonized, required interpolating GOSE outcomes in studies using different scales, a method supported by prior literature[67] but nonetheless subject to estimation bias. Additionally, the cumulative GOSE framework employed is descriptive rather than inferential and does not account for important confounders such as institutional protocols, prehospital care, or cranioplasty timing.

Despite these limitations, our findings suggest that institutional factors, such as early surgical decision-making, ICP-targeted care, and integrated post-acute planning, may synergistically contribute to improved outcomes, even in the absence of statistically significant predictors at the individual patient level. These results support a move toward structured, individualized pathways that go beyond acute survival and prioritize long-term recovery and reintegration.

5.5 Suggestions for Future Research

The present study has offered a retrospective evaluation of DC in a heterogeneous cohort of pediatric patients treated at the University Hospital of Padua, with the dual aim of assessing outcome trends and exploring potential prognostic factors. Although the small sample size and single-center scope limited inferential power, the integration of cumulative GOSE-based comparisons and the review of five relevant international studies provide a solid foundation upon which to build future investigation.

In line with our aim, a key priority for future research is the expansion of this analysis into a prospective, multicenter framework. A multicenter registry would allow for standardization in data collection, particularly regarding outcome measurement timing, follow-up duration, and post-discharge rehabilitation, which varied substantially across the literature and often limited comparability.

Second, while initial GCS was reaffirmed as a strong prognostic marker, most other variables (age, etiology, radiological features, DC timing) lacked predictive value in isolation. Future research should thus employ multivariate models combining clinical, radiologic, and physiological data (e.g., ICP, CPP, sedation depth), specifically validated in pediatric cohorts.

Another clear priority is the refinement of outcome assessment tools. Although GOSE-Peds is validated, it does not fully capture neurocognitive or psychosocial sequelae. Incorporating instruments such as the Pediatric Quality of Life Inventory (PedsQL),[86] the Child Behavior Checklist (CBCL)[87], and structured neuropsychological testing batteries into long-term follow-up would allow for a more deep understanding of recovery trajectories. In parallel, caregiver-reported outcomes and school reintegration success should be systematically monitored.

Additionally, the comparable outcomes between traumatic and non-traumatic etiologies in this and other recent studies suggest the need for etiology-specific analyses, to identify modifiable predictors within subgroups.

Given the persistent uncertainty around optimal timing of DC, especially in secondary procedures, future research should also focus on defining time-dependent thresholds using high-resolution physiological monitoring (e.g., ICP,

brain tissue oxygenation). Similarly, the timing and neurological impact of cranioplasty, including its effects on seizures and neurodevelopment, deserve dedicated study.

Finally, to support evidence-based care, future research should include implementation science components: examining institutional variability in protocols, access to rehabilitation, and decision-making. International collaborations and the creation of standardized pediatric DC registries (e.g. through EANS or ESPN) would facilitate this effort and allow for benchmarking outcomes across centers.

6 CONCLUSIONS

Decompressive craniectomy remains a valuable life-saving intervention in pediatric patients with elevated intracranial pressure due to diverse etiologies. Our findings confirm that functional outcomes after DC are not determined by any single clinical, radiological, or surgical factor, but rather emerge from the interplay of multiple dynamic variables, including initial neurological status, monitoring strategies, surgical timing, and post-acute rehabilitation. Thus. The study confirms that favorable neurological recovery is possible across a range of etiologies, particularly when surgery is embedded within a comprehensive and structured care strategy.

Despite the absence of statistically significant predictors for complications or unfavorable outcomes, certain trends, such as the benefit of early ICP-guided management and the non-inferiority of non-traumatic etiologies, underscore the importance of contextual, protocol-driven care over rigid prognostic models. The comparison with existing literature suggests that early surgical intervention, multimodal monitoring, and streamlined cranioplasty pathways may contribute to improved recovery trajectories.

Nevertheless, achieving optimal outcomes in pediatric neurotrauma extends beyond acute survival. Our data reinforce the need for long-term, multidimensional follow-up strategies that address neurocognitive, behavioral, and psychosocial recovery. Future multicenter prospective studies with larger cohorts and integrated outcome assessments are essential to refine prognostic models and further optimize care pathways in the pediatric population.

7 BIBLIOGRAPHY

1. Menon DK, Schwab K, Wright DW, Maas AI, Demographics and Clinical Assessment Working Group of the International and Interagency Initiative toward Common Data Elements for Research on Traumatic Brain Injury and Psychological Health. Position statement: definition of traumatic brain injury. Arch Phys Med Rehabil. 2010 Nov;91(11):1637–40.

2. Dewan MC, Mummareddy N, Wellons JC, Bonfield CM. Epidemiology of Global Pediatric Traumatic Brain Injury: Qualitative Review. World Neurosurg. 2016 Jul;91:497-509.e1.

3. The Epidemiology of Traumatic Brain Injury in Children and Youths: A Review of Research Since 1990 | Request PDF. ResearchGate [Internet]. 2025 Mar 7 [cited 2025 Jun 11]; Available from: https://www.researchgate.net/publication/264833554_The_Epidemiology_of_Traumatic_Brain_Injury_in_Children_and_Youths_A_Review_of_Research_Since_1990

4. Flanagan SR. Invited Commentary on “Centers for Disease Control and Prevention Report to Congress: Traumatic Brain Injury in the United States: Epidemiology and Rehabilitation.” Archives of Physical Medicine and Rehabilitation. 2015 Oct;96(10):1753–5.

5. Servadei F, Begliomini C, Gardini E. Incidence of Traumatic Brain Injury in Italy. J Neurosurg Sci. 2002;

6. Castelão M, Lopes G, Vieira M. Epidemiology of major paediatric trauma in a European Country – trends of a decade. BMC Pediatr. 2023 Apr 25;23(1):194.

7. Da Dalt L, Parri N, Amigoni A, on behalf of the Italian Society of Pediatric Emergency Medicine (SIMEUP), the Italian Society of Pediatrics (SIP), Nocerino A, et al. Italian guidelines on the assessment and management of pediatric head injury in the emergency department. Ital J Pediatr. 2018 Dec;44(1):7.

8. Kemp AM, Stoodley N, Cobley C, Coles L, Mann M, Rolfe K, et al. Appearances of subdural hemorrhage associated with non-accidental head injury in children: A review of 56 cases. Clinical Radiology. 1999;54(11):702–8.

9. Oehmichen M, Meissner C, König HG. Brain damage after acute subarachnoid hemorrhage (SAH): Pathomorphology and forensic aspects. Journal of Neurotrauma. 2006;23(10):1532–42.

10. Langlois JA, Rutland-Brown W, Thomas KE. Traumatic Brain Injury in the United States: Emergency Department Visits, Hospitalizations, and Deaths. Atlanta, GA: Centers for Disease Control and Prevention; 2006.

11. Figueiredo EG, Welling LC, Rabelo NN, editors. Neurocritical Care for Neurosurgeons: Principles and Applications [Internet]. Cham: Springer International Publishing; 2021 [cited 2025 Jun 11]. Available from: https://link.springer.com/10.1007/978-3-030-66572-2

12. Piatt JHJr. Intraventricular hemorrhage in infancy: Management and outcome. Child's Nervous System. 1992;8(2):63–9.

13. Adams JH, Graham DI, Murray LS, Scott G. Diffuse axonal injury due to nonmissile head injury in humans: An analysis of 45 cases. Annals of Neurology. 1982;12(6):557–63.

14. Zucchelli M, Cama A, Consales A. Abusive Head Trauma: A Review. Frontiers in Neurology. 2020;11:118.

15. Giustini A, Pistarini C, Pisoni C. Traumatic and nontraumatic brain injury. In: Handbook of Clinical Neurology [Internet]. Elsevier; 2013 [cited 2025 Jun 14]. p. 401–9. Available from: https://linkinghub.elsevier.com/retrieve/pii/B9780444529015000344

16. Ferriero DM. Neonatal brain injury. New England Journal of Medicine. 2004;351(19):1985–95.

17. Ramaswamy V, Miller SP, Barkovich AJ, others. Perinatal stroke. Seminars in Fetal and Neonatal Medicine. 2009;14(5):248–55.

18. Jordan LC, Hillis AE. Hemorrhagic stroke in children. Pediatric Neurology. 2011;45(4):243–52.

19. Ganesan V, Hogan A, Shack N, others. Outcome after ischemic stroke in childhood. Developmental Medicine and Child Neurology. 2000;42(7):455–61.

20. Sébire G, Tabarki B, Saunders DE, others. Cerebral venous sinus thrombosis in children: risk factors, presentation, diagnosis and outcome. Brain. 2005;128(Pt 3):477–89.

21. Shankaran S, Laptook AR, Ehrenkranz RA, others. Whole-body hypothermia for neonates with hypoxic–ischemic encephalopathy. New England Journal of Medicine. 2005;353(15):1574–84.

22. Hersh DS, Groves MLA. DECOMPRESSIVE CRANIECTOMY IN PEDIATRIC TBI.

23. Aldrich EF, Eisenberg HM, Saydjari C, others. Outcome following severe head injury in children: The National Pediatric Trauma Registry. Journal of Neurosurgery. 1992;76(3):437–44.

24. Pinto PS, Poretti A, Meoded A, Tekes A, Huisman TAGM. The Unique Features of Traumatic Brain Injury in Children. Review of the Characteristics of the Pediatric Skull and Brain, Mechanisms of Trauma, Patterns of Injury, Complications and Their Imaging Findings—Part 1. Journal of Neuroimaging [Internet]. 2012 Apr [cited 2025 Jun 11];22(2). Available from: https://onlinelibrary.wiley.com/doi/10.1111/j.1552-6569.2011.00688.x

25. Patel JJ. Cerebral Metabolism. In: Freeman BS, Berger JS, editors. Anesthesiology Core Review: Part Two Advanced Exam [Internet]. New York, NY: McGraw-Hill Education; 2016. Available from: accessanesthesiology.mhmedical.com/content.aspx?aid=1135738838

26. Raboel PH, Bartek J, Andresen M, Bellander BM, Romner B. Intracranial Pressure Monitoring: Invasive versus Non-Invasive Methods—A Review. Critical Care Research and Practice. 2012;2012:1–14.

27. Harary M, Dolmans RGF, Gormley WB. Intracranial Pressure Monitoring—Review and Avenues for Development. Sensors. 2018 Feb 5;18(2):465.

28. Mokri B. The Monro–Kellie hypothesis: Applications in CSF volume depletion. Neurology. 2001 Jun 26;56(12):1746–8.

29. Rosengart AJ. Recognition and Management of Intracranial Hypertension. Intracranial Hypertension.

30. Canac N, Jalaleddini K, Thorpe SG, Thibeault CM, Hamilton RB. Review: pathophysiology of intracranial hypertension and noninvasive intracranial pressure monitoring. Fluids Barriers CNS. 2020 Dec;17(1):40.

31. Mallard C, Ek CJ, Vexler ZS. The myth of the immature barrier systems in the developing brain: role in perinatal brain injury. J Physiol. 2018 Dec;596(23):5655–64.

32. Sankhyan N, Vykunta Raju KN, Sharma S, Gulati S. Management of Raised Intracranial Pressure. Indian J Pediatr. 2010 Dec;77(12):1409–16.

33. Desforges JF, White RJ, Likavec MJ. The Diagnosis and Initial Management of Head Injury. N Engl J Med. 1992 Nov 19;327(21):1507–11.

34. Reilly PL, Simpson DA, Sprod R, Thomas L. Assessing the conscious level in infants and young children: a paediatric version of the Glasgow Coma Scale. Child's Nerv Syst. 1988 Feb;4(1):30–3.

35. Borgialli DA, Mahajan P, Hoyle JD, Powell EC, Nadel FM, Tunik MG, et al. Performance of the Pediatric Glasgow Coma Scale Score in the Evaluation of Children With Blunt Head Trauma. Walthall J, editor. Academic Emergency Medicine. 2016 Aug;23(8):878–84.

36. Fernando SM, Tran A, Cheng W, Rochwerg B, Taljaard M, Kyeremanteng K, et al. Diagnosis of elevated intracranial pressure in critically ill adults: systematic review and meta-analysis. BMJ. 2019 Jul 24;366:l4225.

37. Kochanek PM, Tasker RC, Carney N, Totten AM, Adelson PD, Selden NR, et al. Guidelines for the Management of Pediatric Severe Traumatic Brain Injury,

Third Edition: Update of the Brain Trauma Foundation Guidelines. Pediatric Critical Care Medicine. 2019 Mar;20(3S):S1–82.

38. Cameron S, Gillio-Meina C, Ranger A, Choong K, Fraser DD. Collection and Analyses of Cerebrospinal Fluid for Pediatric Translational Research. Pediatric Neurology. 2019 Sep;98:3–17.

39. Lyons MK, Meyer FB. Cerebrospinal Fluid Physiology and the Management of Increased Intracranial Pressure. Mayo Clinic Proceedings. 1990 May;65(5):684–707.

40. Stocchetti N, Maas AIR. Traumatic Intracranial Hypertension. N Engl J Med. 2014 May 29;370(22):2121–30.

41. Evensen KB, Eide PK. Measuring intracranial pressure by invasive, less invasive or non-invasive means: limitations and avenues for improvement. Fluids Barriers CNS. 2020 Dec;17(1):34.

42. Moraes FMD, Silva GS. Noninvasive intracranial pressure monitoring methods: a critical review. Arq Neuro-Psiquiatr. 2021 May;79(5):437–46.

43. Ali HT, Sula I, AbuHamdia A, Elejla SA, Elrefaey A, Hamdar H, et al. Nervous System Response to Neurotrauma: A Narrative Review of Cerebrovascular and Cellular Changes After Neurotrauma. J Mol Neurosci. 2024 Feb 17;74(1):22.

44. Tasker RC. UpToDate. Available from: https://www.uptodate.com/contents/elevated-intracranial-pressure-icp-in-children-management?search=intracranial%20hypertension%20management%20pediatric&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1

45. Pittman T, Bucholz R, Williams D. Efficacy of Barbiturates in the Treatment of Resistant Intracranial Hypertension in Severely Head-Injured Children. Pediatr Neurosurg. 1989;15(1):13–7.

46. Stevens RD, Shoykhet M, Cadena R. Emergency Neurological Life Support: Intracranial Hypertension and Herniation. Neurocrit Care. 2015 Dec;23(S2):76–82.

47. Moon JW, Hyun DK. Decompressive Craniectomy in Traumatic Brain Injury: A Review Article. Korean J Neurotrauma. 2017;13(1):1.

48. Bartlett HH, Huie K, Ginalis E, Jumah F, Raju B, Nanda A. Legacies of Neurosurgery and its Implications on Global Neurosurgery Today. World Neurosurgery. 2021 Nov;155:115–21.

49. Cooper PR, Rovit RL, Ransohoff J. Hemicraniectomy in the treatment of acute subdural hematoma: a re-appraisal. Surg Neurol. 1976 Jan;5(1):25–8.

50. Guerra WKW, Gaab MR, Dietz H, Mueller JU, Piek J, Fritsch MJ. Surgical decompression for traumatic brain swelling: indications and results. Journal of Neurosurgery. 1999 Feb;90(2):187–96.

51. Münch E, Horn P, Schürer L, Piepgras A, Paul T, Schmiedek P. Management of Severe Traumatic Brain Injury by Decompressive Craniectomy. Neurosurgery. 2000 Aug 1;47(2):315–23.

52. Rossini Z, Nicolosi F, Kolias AG, Hutchinson PJ, De Sanctis P, Servadei F. The History of Decompressive Craniectomy in Traumatic Brain Injury. Front Neurol. 2019 May 8;10:458.

53. Cooper DJ, Rosenfeld JV, Murray L, Arabi YM, Davies AR, D'Urso P, et al. Decompressive Craniectomy in Diffuse Traumatic Brain Injury. N Engl J Med. 2011 Apr 21;364(16):1493–502.

54. Hutchinson PJ, Kolias AG, Timofeev IS, Corteen EA, Czosnyka M, Timothy J, et al. Trial of Decompressive Craniectomy for Traumatic Intracranial Hypertension. N Engl J Med. 2016 Sep 22;375(12):1119–30.

55. Hawryluk GWJ, Rubiano AM, Totten AM, O'Reilly C, Ullman JS, Bratton SL, et al. Guidelines for the Management of Severe Traumatic Brain Injury: 2020 Update of the Decompressive Craniectomy Recommendations. Neurosurg. 2020 Sep;87(3):427–34.

56. Al-Jishi A, Saluja RS, Al-Jehani H, Lamoureux J, Maleki M, Marcoux J. Primary or Secondary Decompressive Craniectomy: Different Indication and Outcome. Can J Neurol Sci. 2011 Jul;38(4):612–20.

57. Solomou G, Sunny J, Mohan M, Hossain I, Kolias AG, Hutchinson PJ. Decompressive craniectomy in trauma: What you need to know. J Trauma Acute Care Surg. 2024 Oct;97(4):490–6.

58. Jaradat A, Al Barbarawi MM, Jamous M, Jarrar S, Daoud SS, Rawabdeh SA, et al. Early versus Late Decompressive Craniectomy in Pediatrics with Traumatic Brain Injuries: A Retrospective Study. World Neurosurgery. 2025 Apr;196:123827.

59. Beucler N, Aurore S, Dagain A. Ideal bone landmarks for optimization of the bone flap in supratentorial unilateral decompressive craniectomy. Neurochirurgie. 2022 Dec;69.

60. Shafiei M, Sourani A, Saboori M, Aminmansour B, Mahram S. Comparison of subcutaneous pocket with cryopreservation method for storing autologous bone flaps in developing surgical wound infection after Cranioplasty: A randomized clinical trial. Journal of Clinical Neuroscience. 2021 Sep;91:136–43.

61. Veldeman M, Geiger M, Clusmann H. How I do it—the posterior question mark incision for decompressive hemicraniectomy. Acta Neurochir. 2021 May;163(5):1447–50.

62. Gopalakrishnan MS, Shanbhag NC, Shukla DP, Konar SK, Bhat DI, Devi BI. Complications of Decompressive Craniectomy. Front Neurol. 2018 Nov 20;9:977.

63. Martin KD, Franz B, Kirsch M, Polanski W, Von Der Hagen M, Schackert G, et al. Autologous bone flap cranioplasty following decompressive craniectomy is combined with a high complication rate in pediatric traumatic brain injury patients. Acta Neurochir. 2014 Apr;156(4):813–24.

64. Bonow RH, Oron AP, Hanak BW, Browd SR, Chesnut RM, Ellenbogen RG, et al. Post-Traumatic Hydrocephalus in Children: A Retrospective Study in

42 Pediatric Hospitals Using the Pediatric Health Information System. NEUROSURGERY. 2018 Oct;83(4):732–9.

65. Bruns N, Kamp O, Lange K, Lefering R, Felderhoff-Müser U, Dudda M, et al. Functional Short-Term Outcomes and Mortality in Children with Severe Traumatic Brain Injury: Comparing Decompressive Craniectomy and Medical Management. Journal of Neurotrauma. 2022 Jul 1;39(13–14):944–53.

66. Nagy L, Morgan RD, Collins RA, Kharbat AF, Garza J, Belirgen M. Impact of timing of decompressive craniectomy on outcomes in pediatric traumatic brain injury. Surgical Neurology International. 2023 Dec 22;14:436.

67. Jagannathan J, Okonkwo DO, Dumont AS, Ahmed H, Bahari A, Prevedello DM, et al. Outcome following decompressive craniectomy in children with severe traumatic brain injury: a 10-year single-center experience with long-term follow up. Journal of Neurosurgery: Pediatrics. 2007 Apr;106(4):268–75.

68. Carballo-Cuello C, De Jesus O, Fernandez-de Thomas RJ, Garcia M, Vigo-Prieto J, De Jesus-Espinosa A. Posttraumatic Hydrocephalus in Pediatric Patients After Decompressive Craniectomy. World Neurosurgery. 2020 Apr;136:e690–4.

69. Iaccarino C, Kolias AG, Roumy LG, Fountas K, Adeleye AO. Cranioplasty Following Decompressive Craniectomy. Front Neurol. 2020 Jan 29;10:1357.

70. Wilson JTL, Pettigrew LEL, Teasdale GM. Structured Interviews for the Glasgow Outcome Scale and the Extended Glasgow Outcome Scale: Guidelines for Their Use. Journal of Neurotrauma. 1998 Aug;15(8):573–85.

71. Wilson L, Boase K, Nelson LD, Temkin NR, Giacino JT, Markowitz AJ, et al. A Manual for the Glasgow Outcome Scale-Extended Interview. Journal of Neurotrauma. 2021 Sep 15;38(17):2435–46.

72. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021 Mar 29;n71.

73. Williams V, Bansal A, Jayashree M, Ismail J, Aggarwal A, Gupta S, et al. Decompressive craniectomy in pediatric non-traumatic intracranial hypertension: a single center experience. British Journal of Neurosurgery. 2020 May 3;34(3):258–63.

74. Taşkapılıoğlu MO. Restrospective analysis of decompressive craniectomy patients due to acute subdural hematoma at pediatric age group. Ulus Travma Acil Cerrahi Derg [Internet]. 2018 [cited 2025 Jun 17]; Available from: https://www.journalagent.com/travma/pdfs/UTD_25_4_383_388.pdf

75. Semenova ZB, Meshcheryakov S, Lukyanov V, Arsenyev S. Decompressive Craniectomy for Traumatic Intracranial Hypertension in Children. In: Depreitere B, Meyfroidt G, Güiza F, editors. Intracranial Pressure and Neuromonitoring XVII [Internet]. Cham: Springer International Publishing; 2021 [cited 2025 Jun 17]. p. 109–13. (Acta Neurochirurgica Supplement; vol. 131). Available from: https://link.springer.com/10.1007/978-3-030-59436-7_23

76. Hubertus V, Finger T, Drust R, Al Hakim S, Schaumann A, Schulz M, et al. Severe Traumatic Brain Injury in children—paradigm of decompressive craniectomy compared to a historic cohort. Acta Neurochir. 2022 May;164(5):1421–34.

77. Korhonen TK, Suo-Palosaari M, Serlo W, Lahtinen MJ, Tetri S, Salokorpi N. Favourable long-term recovery after decompressive craniectomy: the Northern Finland experience with a predominantly adolescent patient cohort. Childs Nerv Syst. 2022 Sep;38(9):1763–72.

78. Fitzgerald E, Donaldson L, Hammond N, Johnson B, Leung KY, McBain R, et al. Methods of functional outcome assessment in neurocritical care trials: A systematic review and meta-analysis. Australian Critical Care. 2025 Mar;38(2):101124.

79. Teasdale GM, Pettigrew LEL, Wilson JTL, Murray G, Jennett B. Analyzing Outcome of Treatment of Severe Head Injury: A Review and Update on Advancing the Use of the Glasgow Outcome Scale. Journal of Neurotrauma. 1998 Aug;15(8):587–97.

80. Appelboom G, Zoller SD, Piazza MA, Szpalski C, Bruce SS, McDowell MM, et al. Traumatic brain injury in pediatric patients: evidence for the effectiveness of decompressive surgery. FOC. 2011 Nov;31(5):E5.

81. Luz Teixeira T, Peluso L, Banco P, Njimi H, Abi-Khalil L, Chanchay Pillajo M, et al. Early Pupillometry Assessment in Traumatic Brain Injury Patients: A Retrospective Study. Brain Sciences. 2021 Dec 20;11(12):1657.

82. Pérez-Bovet J, Garcia-Armengol R, Buxó-Pujolràs M, Lorite-Díaz N, Narváez-Martínez Y, Caro-Cardera JL, et al. Decompressive craniectomy for encephalitis with brain herniation: case report and review of the literature. Acta Neurochir. 2012 Sep;154(9):1717–24.

83. Keller E, Pangalu A, Fandino J, Könü D, Yonekawa Y. Decompressive craniectomy in severe cerebral venous and dural sinus thrombosis. In: Yonekawa Y, Keller E, Sakurai Y, Tsukahara T, editors. New Trends of Surgery for Stroke and its Perioperative Management [Internet]. Vienna: Springer-Verlag; 2005 [cited 2025 Jun 20]. p. 177–83. (Acta Neurochirurgica Supplements; vol. 94). Available from: http://link.springer.com/10.1007/3-211-27911-3_28

84. Anderson V, Catroppa C, Morse S, Haritou F, Rosenfeld J. Functional plasticity or vulnerability after early brain injury? 2005 Dec;

85. Babikian T, Asarnow R. Neurocognitive outcomes and recovery after pediatric TBI: Meta-analytic review of the literature. Neuropsychology. 2009 May;23(3):283–96.

86. James W. Varni, Ph.D. The PedsQl™ Measurement Model for the Pediatric Quality of Life Inventory™.

87. Hayman-Abello SE, Rourke BP, Fuerst DR. Psychosocial status after pediatric traumatic brain injury: A subtype analysis using the Child Behavior Checklist. J Int Neuropsychol Soc. 2003 Sep;9(6):887–98.