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OUTCOME OF EARLY CRANIOPLASTY IN TREPHINE SYNDROME OR PARADOXICAL BRAIN HERNIATION: SYSTEMATIC REVIEW

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Abstract

Background: Cranioplasty (CP) following decompressive craniectomy (DC) restores skull integrity, improves intracranial physiology, and addresses complications such as sinking skin flap syndrome (SSS) and paradoxical brain herniation (PBH). Historically delayed for months to minimize infection risk, the optimal timing of CP remains controversial. Recent literature suggests that early CP (≤3 months) may improve neurological outcomes without increasing peri-operative complications.

Objective: This systematic review aimed to determine whether early CP improves neurological recovery and peri-operative safety compared with delayed CP, and to examine its role in reversing SSS and PBH.

Methods: A comprehensive search of PubMed, Scopus, Web of Science, and LILACS (January 2000–June 2025) identified comparative studies, observational cohorts, and case reports on CP timing. Two reviewers independently screened, extracted data, and assessed risk of bias using ROBINS-I and Newcastle–Ottawa scales. Heterogeneity precluded quantitative pooling; therefore, a narrative synthesis was performed.

Results: Twelve studies met inclusion criteria, including ten cohorts (n = 77–159 each) and two case reports. Definitions of early CP varied from <30 days to <90 days. Overall complication rates ranged from 19% to 44%. Most cohorts reported comparable infection rates between early and delayed CP, with some showing lower infection rates and significantly shorter operative times in early groups. Several studies suggested reduced hydrocephalus rates with ultra-early CP (<30 days). Neurological recovery improved after CP in both early and late groups, though earlier intervention sometimes yielded faster functional gains. Case reports and small series demonstrated rapid reversal of SSS and PBH following CP. Predictive modeling indicated that older age, low pre-operative GCS, larger defect area, and longer DC-to-CP intervals predicted worse outcomes.

Conclusion: Early CP appears safe and may provide advantages in operative efficiency, hydrocephalus prevention, and neurological recovery, particularly in selected patients after TBI. In the presence of SSS or PBH, expedited CP should be strongly considered. Large, prospective, and etiology-specific studies are needed to refine optimal timing.

Background

Cranioplasty (CP) is the surgical restoration of skull integrity after a decompressive craniectomy (DC). DC is performed to control refractory intracranial hypertension after traumatic brain injury (TBI), stroke or other causes of cerebral oedema. By removing a skull segment, DC creates space for the swollen brain, reducing intracranial pressure and improving cerebral perfusion [1]. Survival benefits from DC have been demonstrated in several randomized trials for malignant middle cerebral artery infarction and severe TBI, leading to its increased utilization in the past two decades [1]. Patients who survive DC usually require subsequent reconstruction of the skull to protect the brain, normalize intracranial physiology and improve cosmesis [1]. Cranioplasty restores the fixed volume of the cranial vault, stabilizes the atmospheric–intracranial pressure gradient and allows brain tissue to re-expand [2], resulting in improved cerebral blood flow and cerebrospinal fluid hydrodynamics. Restoration of skull integrity has been associated with improvements in neurological function, cognition and quality of life, although the exact mechanisms remain uncertain [1].

Cranioplasty also addresses complications unique to the post-craniectomy state. Paradoxical brain herniation (also known as sinking skin flap syndrome or syndrome of the trephined) is a rare but potentially fatal complication of DC [2]. It occurs when atmospheric pressure exceeds intracranial pressure, resulting in displacement of brain tissue and midline shift through intracranial boundaries; it may be triggered by cerebrospinal fluid drainage or lumbar puncture [2]. Clinically, patients may develop motor weakness, cognitive deficits, language disturbance, altered consciousness and headaches, often months after DC [1]. Management involves restoring intracranial pressure (Trendelenburg positioning, adjusting CSF drainage) and performing cranioplasty [2]. Similarly, the syndrome of the trephined (SoT) refers to delayed neurological decline after DC that resolves following CP; SoT is probably due to negative pressure gradients and impaired CSF dynamics. In addition, CP is sometimes undertaken urgently to treat paradoxical herniation or sinking skin syndrome [1].

Historically, CP was delayed for several months to allow cerebral oedema to subside and to reduce infection risk. Recent studies challenge this dogma. A narrative review indicated that early CP (within three months) may enhance neurological recovery and that infection rates are comparable with delayed CP. An international consensus meeting defined four timing categories: ultra-early (≤ 6 weeks), early (6 weeks–3 months), intermediate (3–6 months) and delayed (> 6 months). Several systematic reviews report complication rates between 15 % and 30 %, with infection historically feared but not consistently increased by early CP [1]. Nonetheless, the optimal timing of CP and its influence on neurological outcomes remain debated. Existing randomized trials of CP timing are lacking; evidence comes mainly from observational cohorts with heterogeneous indications, patient populations and definitions of "early".

Objectives

Primary objective: To determine whether early cranioplasty (≤ 3 months after decompressive craniectomy) improves outcomes compared with later cranioplasty (> 3 months) in adults who have undergone DC for TBI, stroke or other causes. Outcomes include neurological recovery, complications (infection, hydrocephalus, hemorrhage, bone resorption) and occurrence of trephine syndrome or paradoxical brain herniation.

Secondary objectives: To explore predictors of favorable or unfavorable outcomes after early CP, to assess the incidence and reversal of SoT and paradoxical herniation after CP, and to identify knowledge gaps for future research

LITERATURE REVIEW

Existing knowledge and gaps:

Historical reports of CP date back to antiquity. Modern CP materials include autologous bone and synthetic implants; autologous bone is often stored subcutaneously or cryopreserved. Material choice may affect infection or resorption rates, but evidence remains inconclusive. A prevailing belief that delayed CP reduces infection risk led to practices of performing CP 6–12 months after DC [1]. However, contemporary reviews suggest that early CP may shorten operative time and hospital stay and may enhance functional recovery [3]. Observational studies indicate overall complication rates between 19 % and 35 %, with infection, hematoma and hydrocephalus being most frequent [1]. A 2018 systematic review found that early CP within 90 days improved motor function but not cognitive outcomes [3]. Nevertheless, the review noted heterogeneity in definitions and low-quality evidence.

Pathophysiological rationale for early CP:

Following DC, there is a negative atmospheric–intracranial pressure gradient and disturbance of CSF circulation; CP re-establishes the fixed cranial vault, improves cerebral blood flow and CSF hydrodynamics. Early restoration may reverse SoT and paradoxical herniation. Because neurological recovery continues for months to years after brain injury, delaying CP may postpone potential benefits during rehabilitation [1,2].

Conflicting evidence:

The observational cohorts summarized in the evidence table demonstrate heterogeneous findings. Several studies (Brommeland 2013, Piedra 2014, Lash 2022, Zhang 2025) report no increase or even reductions in complications with early CP. Others (Kim 2020) observed higher infection rates with very early CP [4]. Many cohorts lacked adjustment for confounders; some defined early CP as < 90 days, whereas others used < 30 days. Few studies

specifically assessed trephine syndrome or paradoxical herniation, and definitions varied. Risk-of-bias assessments indicate that most evidence is at moderate or high risk of bias because of retrospective designs and confounding. The absence of randomized trials leaves uncertainty about causality. Moreover, there is limited data on the effect of CP timing in patients with different indications (TBI vs stroke) or with pre-existing hydrocephalus or infection. Regional differences in rehabilitation pathways may also affect outcomes, yet few studies account for these factors. There is a paucity of high-quality data from Africa or low-income regions; most evidence comes from high-income countries. Additional prospective, multicenter studies and randomized trials are needed.

METHODS

Protocol and registration: This systematic review followed PRISMA 2020 and the Cochrane Handbook (v6.4).

Eligibility criteria: We included human studies published between 1 January 2000 and 30 June 2025 that examined the timing of cranioplasty after decompressive craniectomy. Eligible designs comprised randomized or quasi-experimental trials, cohort studies, case–control studies and analytical cross-sectional studies. Case reports and case series were included only when they described trephine syndrome or paradoxical herniation with timing details. Studies without primary data, editorials, letters and reviews were excluded. No language restrictions were applied; non-English articles were translated.

Information sources and search strategy: Searches were conducted on PubMed, Scopus, Web of Science, LILACS on 30 June 2025. Controlled vocabulary (e.g., MeSH for PubMed) and free-text terms were combined using Boolean operators. The PubMed search string (see appendix) included terms for decompressive craniectomy, cranioplasty, timing and trephine syndrome. Equivalent strings were constructed for other databases using appropriate field codes (e.g., TITLE-ABS-KEY for Scopus). Also, Scopus and Web of Science were examined too; LILACS was searched in Spanish and Portuguese. Reference lists of included articles and relevant reviews were manually screened for additional studies.

Selection process: Two reviewers independently screened titles and abstracts. Full texts of potentially eligible articles were retrieved and assessed for inclusion. Disagreements were resolved by discussion. Reasons for exclusion at the full-text stage were recorded.

Data extraction: A standardized form captured study characteristics (country, design, sample size, indication), timing of CP, outcomes (neurological scores, complications, mortality, occurrence of trephine syndrome/paradoxical herniation) and effect estimates (mean ± SD, odds ratios). When data were missing, authors were not contacted, and "NR" was recorded. Extraction was performed by one reviewer and verified by a second.

Table (1): PRISMA 2020 flow diagram numeric summary

Stage	Exact count	Notes
Records retrieved (multi-database)	**3962**	Searches were run on PubMed, Scopus, Web of Science and the regional index LILACS for studies published between 1 January 2000 and 30 June 2025. Boolean strings combining MeSH/Emtree terms and free-text synonyms for decompressive craniectomy and cranioplasty were used. The PubMed search retrieved 896 records, while combined Scopus/Web of Science/LILACS coverage returned 3066 additional records, giving 3962 records.
After automatic deduplication	**3621**	Duplicate DOIs and titles were removed using reference-management software, reducing the set to 3621 unique records.
After manual deduplication	**3574**	Manual review excluded conference abstracts, editorials and letters duplicated under different formats.
Records excluded after title/abstract screening	**3 544**	Titles/abstracts were screened in duplicate. Records were excluded for being irrelevant (animal studies, pediatric non-comparative case reports or topics unrelated to cranioplasty timing/complications).
Full-text articles assessed for eligibility	**30**	Thirty articles were obtained in full. Four texts were unavailable in English; these were translated using online translation tools.
Studies included in final evidence table	**12**	Twelve primary studies met the inclusion criteria.

Top 3 reasons for full-text exclusion	**Not comparative (n = 10); lacked timing information (n = 4); duplicate cohort or superseded by later study (n = 4).**	

Risk-of-bias assessment: ROBINS-I and the Newcastle–Ottawa Scale were used for non-randomised studies; judgments were made independently by two reviewers and disagreements resolved by consensus.

Synthesis: Studies were grouped chronologically. Given heterogeneity in designs, definitions of early CP and outcomes, a narrative synthesis was undertaken. Effect estimates were summarized without pooling. Predictors identified in multivariable analyses were tabulated.

RESULTS

Study characteristics: Twelve studies met eligibility criteria, including ten observational cohorts (N = 77–157) and two case reports. Indications for DC included TBI, malignant middle cerebral artery infarction and other strokes. Early CP definitions varied: most defined early as < 3 months, while some defined ultra-early as < 30 days. Delayed CP ranged from ≥ 3 months to > 6 months. Follow-up periods ranged from immediate postoperative to two years.

Complications and outcomes: Overall complication rates ranged from 19 % to 44 %. Infection rates were generally comparable between early and delayed CP groups [5][6], challenging the traditional belief that early surgery increases infection. Several studies reported shorter operative times with early CP [5][6] and lower rates of hydrocephalus [6]. The largest cohort (Piedra 2014) found lower infection (7.7 % vs 14 %) and shorter operative time (102 min vs 125 min) in the early group [7]. Other cohorts (Brommeland 2013, Aloraidi 2021) found no significant differences in complications or neurological outcomes between early and late CP. The Korean study noted increased infection with very early CP but increased hematoma with late CP [4].

Trephine syndrome and paradoxical herniation: Only the Brazilian series explicitly assessed sinking skin syndrome; 17 of 27 patients developed SSS, with onset around 19 days after DC, and 94 % improved following CP[8]. The case report by Zamir 2025 highlighted rapid neurological recovery after CP at six weeks, illustrating SoT reversal [9]. No comparative studies reported the incidence of trephine syndrome by timing category.

Predictors of outcome: The Chinese predictive model identified older age, lower preoperative GCS, higher NIHSS scores, larger defect area and longer interval from DC to CP as predictors of poor outcome [10]. The model's AUC of 0.92 suggests good discrimination [10].

Across studies, early CP (within three months) appears at least as safe as delayed CP and may confer advantages in operative time, hydrocephalus prevention and neurological recovery. Ultra-early CP (< 30 days) remains controversial; small cohort studies suggest it may reduce hydrocephalus without increasing infection [6], but infection risk may be higher if performed too early [4]. The heterogeneity of definitions, small sample sizes and lack of randomized trials limit confidence. The evidence indicates that patient selection based on neurological status, defect size and absence of infection is crucial. The pathophysiological rationale for early CP estoring intracranial pressure and improving cerebral perfusion is supported by case reports and observational improvements [1][2]. However, a high-quality randomized controlled trial is needed to determine the optimal timing of CP and to assess its impact on trephine syndrome, paradoxical herniation, functional outcomes and quality of life.

Table (2): Included evidence table arranged from oldest to newest

Legend: ADL = Activities of Daily Living score; DC = decompressive craniectomy; CP = cranioplasty; mRS = modified Rankin Scale; GOS = Glasgow Outcome Scale; NIHSS = National Institutes of Health Stroke Scale; SSS = sinking skin syndrome; SoT = syndrome of trephined; U = ultra-early (< 30 days) or early (< 3 months).

First author & year	Country/setting	Design & sample (type, N, key criteria)	Intervention/exposure	Main outcome findings	Key conclusion

Gooch et al. 2009	United States; single neurosurgical center	Retrospective cohort; N = 62 adults undergoing CP after DC for various indications (traumatic brain injury and stroke).	Patients underwent CP at median 13 months (late). No comparison with early CP.	Overall complication rate 22 %; infections 8 %; hydrocephalus 8 %; pneumocephalus 6 %; no mortality.	Late CP remains associated with notable complications; study highlights need for timing research.
Brommeland et al. 2013	Norway; tertiary referral hospital	Prospective cohort; N = 42 adults; compared early CP (< 90 d, n = 20) with delayed CP (≥ 90 d, n = 22).	Early CP median 54 d; delayed CP 13 months[.	Complications: early 21 % vs late 30 % (p > 0.05); infection 5 % vs 14 %; hydrocephalus 8 % vs 8 %. Mean hospital stay 77 vs 63 d; no significant differences.	Early CP did not increase complications and may reduce infection.
Piedra et al. 2014	United States; level-1 trauma center	Retrospective cohort; N = 157 trauma patients, early CP < 12 weeks (n = 52) vs late CP ≥ 12 weeks (n = 105).	Early group median time 8 weeks.	Overall complication rate 35 %. Infection 7.7 % (early) vs 14 % (late); bone resorption 15 % vs 19 %; hydrocephalus 7.7 % vs 1.3 %; operative time shorter in early group (102 min vs 125 min).	Early CP had fewer infections and shorter surgery without increased complications; bone resorption higher in younger patients.
Kim et al. 2020	South Korea; academic hospital	Retrospective cohort; N = 109 adults; categorized timing: very early (< 30 d), early (30–60 d), late (60–90 d), more-late (> 90 d).	Indications varied; CP undertaken as soon as clinically feasible.	Overall complication rate 44 %; hydrocephalus 34.9 %; infection 6.4 %; postoperative hematoma 4.6 %. Infection increased with earlier timing; hematoma increased with later timing (p = 0.007). Hydrocephalu	Very early and early CP can be safe but patient selection is critical.

				s associated with indication rather than timing.	
Aloraidi et al. 2021	Saudi Arabia; multi-centre	Retrospective cohort; N = 101; early CP < 90 d (n = 43) vs late ≥ 90 d (n = 58).	Follow-up mean 20 months.	Mean GOS 4.0; mRS 2.2. No significant difference in hydrocephalus (6 vs 12), seizures (12 vs 16) or sunken flap syndrome (0 vs 3). Mortality 1 per group.	Timing did not influence neurological outcomes or complications.
Ultra-early vs conventional CP (Sethi et al. 2022)	United States; Level-1 trauma centre	Retrospective cohort; N = 77; ultra-early CP (< 30 d; n = 29) vs conventional (> 30 d; n = 48).	Ultra-early CP average 17.7 ± 7.8 d; conventional 95.7 ± 65.6 d.	Ultra-early CP shorter operative time (2.40 ± 0.71 h vs 3.00 ± 1.63 h, p = 0.0336); hydrocephalus lower (10.3 % vs 31.6 %, p = 0.026); infection and return-to-OR similar.	Ultra-early CP may reduce hydrocephalus and operative time without increasing infection.
Sinking skin syndrome series (Santander et al. 2022)	Brazil; single hospital	Retrospective case series; N = 27 with large DC; 17 developed SSS.	Mean time from DC to SSS 19 d; CP performed at median 4.1 months in SSS vs 2 months in non-SSS[8].	94 % improved after CP; delayed CP associated with higher SSS incidence.	Delayed CP increases risk of sinking skin syndrome; early CP led to neurological improvement.
Yan et al. 2024.	China; tertiary hospital	Retrospective study; N = 142 early CP cases (< 3 months).	Logistic regression identified age, preoperative GCS, NIHSS, defect area and interval time between DC and CP as predictors of poor outcome.	ORs: age 4.105; preoperative GCS 0.180; NIHSS 3.654; defect area 12.678; interval time 3.780. Predictive model AUC 0.924 (training) and 0.918 (validation).	Provides a tool to select patients for early CP and emphasizes that earlier timing may reduce complications when patients are appropriately selected.
Same cohort of Yan et al. 2024.	China; tertiary hospital	Retrospective cohort; N = 142 CP	Early CP improved ADL scores (RANKIN) at	Main predictors of unfavorable	Early CP within 3 months

		cases < 3 months; compared favourable vs unfavourable outcomes.	1 month; by 3 months differences disappeared.	outcome were large defect area and longer interval; emphasised that early CP can benefit selected patients.	safe and beneficial.
Yan et al. 2025.	China; single centre	Retrospective cohort; N = 86 malignant cerebral infarction patients after DC; early CP (< 3 months; n = 37) vs traditional (> 3 months; n = 49).	Early CP decreased operative time and blood loss; subcutaneous effusion 5.41 % vs 14.29 %; wound infection 5.41 % vs 8.16 %; wound dehiscence 0 % vs 4.08 %; hydrocephalus 5.41 % vs 4.08 %; overall complication 24.32 % vs 28.57 % (p > 0.05).	Early CP is safe, reduces operative time and blood loss, and improves functional outcomes compared with delayed CP.	
Zhao et al. 2025.	China; single centre	Retrospective cohort; N = 159; ultra-early CP (< 3 weeks; n = 23) vs non-ultra-early (> 3 weeks; n = 136).	Ultra-early CP shorter surgery duration; no significant difference in overall complications (17.39 % vs 14.71 %, p = 0.739); no long-term difference in ADL scores.	Ultra-early CP is safe and shortens surgery; recommended in selected patients.	
Ashfaq et al. 2025.	Pakistan; clinical case	Report of a patient with trephine syndrome after DC for traumatic brain injury.	CP performed at 6 weeks post-DC led to rapid improvement in motor strength, cognitive function and reversal of paradoxical brain herniation.	Early CP is definitive treatment for trephine syndrome; emphasises need for high suspicion and timely surgery.	

Table (3): Risk-of-bias assessment
Tool: ROBINS-I (non-randomised studies) or NOS (observational cohorts); there were no randomised trials. Each domain is rated Low, Moderate or High risk of bias.

Study	Bias due to confounding	Bias in participant selection	Bias in classification of inter	Bias due to deviations from inten	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of reported results	Overall risk & justification

			ventions	ded interventions				
Gooch 2009	🔴 High	🟡 Moderate	🟡 Moderate	🟢 Low	🟢 Low	🟡 Moderate	🔴 High	Retrospective design with no comparator; confounders such as severity of injury and comorbidities not controlled; outcome assessment not blinded.
Brommeland 2013	🟡 Moderate	🟡 Moderate	🟢 Low	🟢 Low	🟢 Low	🟡 Moderate	🟡 Moderate	Prospective cohort; some selection bias since timing decided clinically; confounders (e.g., brain injury severity) partially controlled; small sample.
Piedra 2014	🟡 Moderate	🟢 Low	🟢 Low	🟢 Low	🟢 Low	🟡 Moderate	🟡 Moderate	Large retrospective cohort; baseline characteristics imbalanced; confounding adjusted partly in multivariable analysis; outcomes recorded consistently.
Kim 2020	🔴 High	🟡 Moderate	🟢 Low	🟡 Moderate	🟡 Moderate	🔴 High	🟡 Moderate	Multiple timing categories without randomization; small sample; confounding by indication; missing data for some outcomes; heterogeneous follow-up.
Aloraidi 2021	🟡 Moderate	🟢 Low	🟢 Low	🟢 Low	🟢 Low	🟡 Moderate	🟡 Moderate	Retrospective with balanced groups; confounding factors not fully adjusted; outcome assessment via mRS may have inter-rater variability.
Sethi 2022	🟡 Moderate	🟡 Moderate	🟢 Low	🟢 Low	🟢 Low	🟡 Moderate	🟡 Moderate	Retrospective; baseline differences not fully addressed; robust outcome reporting; high hydrocephalus difference suggests unmeasured confounders.
Santander 2022	🔴 High	🔴 High	🟡 Moderate	🟢 Low	🟢 Low	🔴 High	🔴 High	Small case series focusing on SSS; no comparator; high risk of selection and measurement bias; results descriptive.
Yan 2024 (predictive model)	🟡 Moderate	🟢 Low	🟢 Low	🟢 Low	🟢 Low	🟡 Moderate	🟡 Moderate	Retrospective; appropriate statistical modelling; potential residual confounding; external validation limited.
Yan 2024 (cohort)	🟡 Moderate	🟢 Low	🟢 Low	🟢 Low	🟢 Low	🟡 Moderate	🟡 Moderate	Same dataset; similar limitations; study relies on logistic regression without randomization.
Yan 2025	🟡 Moderate	🟢 Low	🟢 Low	🟢 Low	🟢 Low	🟡 Moderate	🟡 Moderate	Retrospective; groups comparable; no significant differences; confounders not completely controlled.
Zhao 2025	🟡 Moderate	🟢 Low	🟢 Low	🟢 Low	🟢 Low	🟡 Moderate	🟡 Moderate	Retrospective; small ultra-early group; confounding likely; outcomes assessed similarly.

Ashfaq 2025	🔴 High	🔴 High	🔴 High	🟢 Low	🟢 Low	🟡 Moderate	🔴 High	Single case report; not comparative; inherently high risk of bias and not generalizable.

DISCUSSION:

The present systematic review set out to determine whether early cranioplasty (CP) defined a priori as ≤3 months after decompressive craniectomy (DC) improves neurological recovery and peri-operative safety compared with later CP, and to examine how timing relates to trephine syndrome/sinking skin flap syndrome (SSS) and paradoxical brain herniation (PBH). In our synthesis of 12 primary studies spanning trauma and stroke populations, early CP was at least as safe as delayed CP, with signals toward shorter operative time and possible reductions in hydrocephalus in ultra-early windows in selected patients.

Across the broader literature, our findings align with multiple systematic reviews concluding that early CP does not meaningfully increase overall complications and may enhance functional recovery. A Surgical Neurology International analysis of trauma cohorts reported that CP within 12 weeks did not raise complication rates versus later surgery and noted longer operative times when CP was delayed beyond 12 weeks [14]. Meta-analytic work focused on complications similarly found no consistent penalty for earlier timing [15], while a complementary meta-analysis pooling standardized neurological scales showed that cranioplasty itself improves function and that earlier procedures were associated with greater post-CP gains than later ones [16]. Together, these data support the biological rationale that restoring the rigid cranial vault early can normalize the atmospheric–intracranial pressure gradient, improve cerebrospinal fluid (CSF) hydrodynamics, and augment cerebral perfusion during a highly plastic phase of recovery.

Individual comparative cohorts echo this pattern. In a 157-patient Level-1 trauma series, early CP (<12 weeks) was associated with significantly shorter operative time (102 vs 125 min) and numerically fewer infections (7.7% vs 14%) compared with later CP (≥12 weeks), without an overall increase in complications (35% in both groups) [14]. Ultra-early series add granularity: at a Level-1 trauma center, CP performed within 30 days yielded shorter operative length and a significantly lower rate of post-CP hydrocephalus versus >30 days, with no differences in infection or return-to-OR events [17]. Conversely, a large single-center review that stratified timing more finely suggested that very early windows may carry a higher infection signal in some contexts, whereas later windows can see more postoperative hematoma highlighting the importance of patient selection and local practice factors [26].

Neutral findings also exist. A multicenter Saudi cohort (n = 101) comparing <90 versus ≥90 days reported no significant differences in modified Rankin Scale (mRS), Glasgow Outcome Score (GOS), hydrocephalus, seizures, or mortality, concluding that timing per se was less influential than readiness (resolution of swelling and adequate soft-tissue condition) [18]. At the meta-analytic level, a 2025 synthesis limited to traumatic brain injury (TBI) found no statistically significant differences in pooled complication rates between ≤90 and >90 days, including for seizures, reinforcing equipoise at that cut-point [27]. These neutral effects likely reflect heterogeneity in indications, definitions of "early," materials, and peri-operative pathways—not necessarily the absence of a timing effect in all subgroups.

Prospective multicenter datasets have recently sharpened the picture. Within CENTER-TBI and Net-QuRe, early (≤90 days) versus delayed (>90 days) CP after DC for TBI showed broadly comparable functional outcomes, emphasizing that when patients are optimized, earlier reconstruction does not compromise recovery; detailed subgroup analyses also explored hydrocephalus and infectious complications without demonstrating a consistent excess risk from early timing [24]. At the same time, single-center experiences help delineate an "ultra-early" lane: a 2025 study of CP performed within 3 weeks reported significantly shorter operative time without a rise in overall complications or long-term activities-of-daily-living scores relative to later CP in appropriately selected candidates [19]. Notably, a separate matched-cohort analysis suggested that compressing timing to within ~60 days may raise morbidity in non-TBI populations, advocating caution outside trauma [25]. The totality of evidence therefore supports an individualized window approach: early CP (6–12 weeks) is generally safe and may be advantageous, while ultra-early CP (≤3–4 weeks) can be considered in select TBI patients within robust peri-operative systems, and greater caution is warranted in malignant infarction and other non-TBI etiologies.

With respect to SSS/PBH, our findings that timely CP reverses neurological deterioration are concordant with focused series and illustrative reports. In a decompressive craniectomy series, SSS was systematically characterized with clinico-radiological correlates, underscoring under-recognition and the pathophysiologic role of impaired CSF flow and venous congestion; improvement after CP was the rule rather than the exception [21]. Case-based literature documents dramatic rescues with urgent CP for life-threatening PBH, with reversal of midline shift and restoration of cisterns within hours on imaging [23]. A recent case with SoT/PBH after infarct also showed rapid recovery after early CP at six weeks, bolstering the concept that timing can be therapeutic, not merely reconstructive [22]. These observations dovetail with our synthesis in which SSS/PBH were indications for expedited reconstruction rather than reasons to delay.

Finally, predictors of outcome can refine selection for earlier surgery. A 2024 outcome-prediction model for early CP identified older age, lower pre-operative GCS, higher NIHSS, larger defect area, and longer DC-to-CP interval as independent risk factors for poor outcome, with strong discrimination on internal validation [20]. Practical implication: in patients with controlled infection risk, favorable wound conditions, and moderate defect size—particularly after TBI—earlier CP can be leveraged to accelerate rehabilitation, while those with large defects, persistent hydrocephalus, or systemic instability may benefit from optimization before reconstruction.

Taken together, the present review suggests three clinical messages. First, in adults after DC, early CP (≈6–12 weeks) is generally not associated with higher infection, seizure, or global complication rates than later CP, and it consistently shortens operative time; several cohorts also suggest fewer downstream CSF disturbances with ultra-early timing when carefully selected [14–18, 27]. Second, early CP can enhance neurological recovery as measured by standardized scales in aggregated analyses, likely by normalizing cranial biomechanics and CSF/cerebral blood flow earlier in the rehabilitation arc [16]. Third, SSS/PBH are compelling indications for expedited CP given the high likelihood of neurological reversal [21–23].

Limitations of the present study warrant caution in interpretation. Our synthesis was necessarily narrative because of heterogeneity in timing definitions (e.g., <30, <60, <90 days), indications (TBI vs. infarction), materials (autologous vs. synthetic), outcome measures, and follow-up horizons, precluding robust pooling. Most included studies were retrospective with moderate-to-high risk of confounding by indication and variable adjustment strategies; ultra-early subgroups were often small. Few studies explicitly measured SSS/PBH incidence across timing categories, and geographic representation was skewed toward high-income settings. Emerging prospective registries and matched analyses provide higher-quality evidence but remain observational [24, 25]. Future work should prioritize randomized or carefully emulated-trial designs stratified by etiology (TBI vs. stroke), standardized timing bins, and core outcome sets (neurological function, hydrocephalus/shunt dependence, infection, quality of life), while prospectively capturing SSS/PBH phenotypes and rehabilitation trajectories.

CONCLUSION:

In conclusion, our review supports early CP as a safe, often beneficial strategy for adults after DC when patients are clinically optimized, with individualized caution in non-TBI etiologies and ultra-early windows. In the presence of SSS/PBH, expedited CP should be strongly considered as definitive therapy.

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