



Cisternostomy in Traumatic Brain Injury for a Novel Approach to Treatment: Review of Current Status

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Abstract

Cisternostomy (CS) is a recently introduced procedure to mitigate the cerebrospinal fluid shift edema and secondary injury in traumatic brain injury patients. There have been numerous reports describing its efficacy in various cohorts of traumatic brain injury (TBI) patients; therefore, we review the current evidences examining its utility for the same. The systematic review was done according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses guideline including all human studies published in English language indexed with MEDLINE and Google Scholar since 2013 evaluating CS as a standalone or as an adjuvant procedure. The studies were graded according to the Oxford center for evidence-based medicine levels of evidence. Case reports were excluded from the analysis. A total of 107 articles were found by using the given search criteria. Finally, three oxford level 3 study and one level 4 study were included in the analysis. CS in combination with decompressive craniectomy was seen to confer mortality benefit and better outcome at discharge. It led to statistically significant improvement in clinical outcome at 6 months in the patients for whom it was performed as a primary procedure. CS is a promising procedure in TBI leading to survival benefit as well as better clinical outcome. But the level of evidence supporting its effectiveness is still weak owing to the methodological limitations and small sample size. A well-designed multicentric randomized controlled trial is needed to critically examine its role in TBI patients.

Keywords

- ▶ cisternostomy
- ▶ traumatic brain injury
- ▶ CSF shift edema
- ▶ Virchow-Robin spaces

Introduction

Traumatic brain injury (TBI) is a critical public health problem worldwide constituting a major cause of mortality and morbidity for people of all ages, but especially in the young age group. With the recent increase in its incidence, injury-related deaths and TBI are projected to be one of the major causes of death and disability by the year 2020.¹ The principle of TBI management centers on the prevention and mitigation of secondary brain injury. However, the progress in its management has not paralleled the progress seen in

other neurosurgical disciplines. The major advances in care of TBI patients have been attributed to the development and evolution of intensive care and neurophysiological monitoring. Initially described by Theodore Kocher, decompressive craniectomy has recently been shown to improve the patient survival while increasing the neurological morbidity.^{2,3}

Originally described by Cherian et al, cisternostomy (CS) has recently been proposed as an effective procedure for TBI management.⁴ It has been shown to be effective both as standalone as well as adjunctive procedure to decompressive craniectomy. CS is defined by opening and drainage of

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subarachnoid basal cistern to atmospheric pressure. The procedure is based on the principle of opening subarachnoidal cisterns leading to opening of paravascular Virchow-Robin spaces resulting in changes in CSF circulation, consequently reducing the CSF shift edema.⁵

Even though an innovative procedure based on a renewed understanding of the pathophysiology of TBI, the evidence supporting the viability and efficacy of procedure is sparse at present. We therefore aim to systematically examine the rationale and effectiveness of CS in TBI population.

Materials and Methods

The systematic review has been done in accordance with the PRISMA guideline (► **Table 1**). Human studies published in English language after 2013 (since the conception of the procedure) addressing the role of CS alone or as adjuvant to decompressive craniectomy in patients

with traumatic brain injury, describing the patient characteristics and outcome were sought. PubMed, MEDLINE, EMBASE, and google scholar search was done from 2013 to 2020, limited to articles published in English language using keywords “CS” (including related keywords like “cisternotomy”) together with traumatic brain injury, TBI, brain injury, and head injury. Non-English language and nonhuman studies were excluded from the analysis. The references of the included articles were searched for potential publications. The studies were evaluated for the TBI patient population, severity of injury, the relevant control group and the procedure performed in each, and postoperative outcomes and complications if any. The outcome was compared with respect to reduction in intracranial pressure (ICP), mortality benefit, improved outcome at 6 weeks or 6 months. The articles included were categorized according to the Oxford Center for Evidence Based Medicine levels of evidence.⁶

Table 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses checklist

Section/topic		Checklist item	Reported on page
Title			
Title	1	Identify the report as a systematic review, meta-analysis, or both	3
Abstract			
Structured summary	2	Provide a structured summary including as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number	1
Introduction			
Rationale	3	Describe the rationale for the review in the context of what is already known	2
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS)	2
Methods			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number	no
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale	3
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched	3
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated	3
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis)	3
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators	3
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made	

(Continued)

Table 1 (Continued)

Section/topic		Checklist item	Reported on page
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis	3
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means)	
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis	
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies)	4–6
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified	
Results			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram	3
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations	3
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12)	
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot	Table 1
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency	
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see item 15)	
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see item 16])	
Discussion			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers)	4–6
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias)	6
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research	6
Funding			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review	

Abbreviation: PICOS, Patients, Intervention, Comparison, and Outcome.

Results

A brief summary of the search result and the study selection process is shown in ► **Fig. 1**. Overall, 107 studies were identified based on the initial search of the database included published between 2013 and 2020. Duplicate studies, case reports, letter to editor, and personal communications and those deemed irrelevant after title and abstract evaluation were removed. Finally, four articles were included in the review process.

The study characteristics and the classification of studies according to the strength of evidence is summarized in ► **Table 2**. Overall, three oxford level 3 study and one level 4 study were identified. There was one prospective nonrandomized controlled trial, two retrospective cohort studies, and one case series exploring the role of CS in severe TBI patients. Two studies compared effect of adjuvant CS to DC with DC alone. One study compared DC with and without adjuvant CS with CS as the only procedure. One case series evaluated the effectiveness of CS as the standalone procedure.

Discussion

Traumatic brain injury can potentially be a grave condition which could be a source of severe morbidity and potentially life threatening. The evolution of TBI depends on the severity of primary injury, which is dependent on the energy transfer to the intracranial structures during the impact as well as secondary brain injury resulting from consecutive injury processes initiated due to the primary damage leading to continued injury and delayed presentation. Secondary injury includes the development of cerebral edema, elevated

ICP, and brain ischemia. The development of post-traumatic cerebral edema has diverse but incompletely understood mechanism. However, the current understanding suggests that cytotoxic edema is the first to develop at the site of injury, which creates a gradient for subsequent trans-capillary movement of fluid resulting in vasogenic edema.⁷ The change in the capillary permeability ensues due to ischemic processes, which along with the build-up of Starling forces is necessary for the development of edema process. It is a sequential process which starts with endothelial dysfunction also known as ionic edema progressing to the breakdown of blood–brain barrier eventually, leading to complete disruption of capillary integrity leading to hemorrhagic conversion.⁷ However, recent development pioneered by Iliff et al⁸ demonstrating the importance of glymphatic system in cerebrospinal fluid (CSF) flow from subarachnoid space through the peri-vascular Virchow-Robin spaces into the brain parenchyma paved the way for improved understanding of the pathophysiology of brain injury. The glymphatic clearance of CSF and solutes was found to decrease by as much as 60% following an episode of TBI.⁹ Therefore, as a consequence of either decreased clearance of interstitial fluid from brain parenchyma or increased CSF influx into parenchyma via peri-vascular spaces there is yet another potential pathway for development and evolution of brain edema postinjury, also known as “CSF-shift edema.”^{5,10-12} The hypothesis concerning “CSF-shift edema” was verified experimentally in a pilot study by Goyal et al, where they found a pressure gradient between the measured cisternal and parenchymal pressures in TBI patients undergoing DC and CS. They demonstrated that immediately following CS,

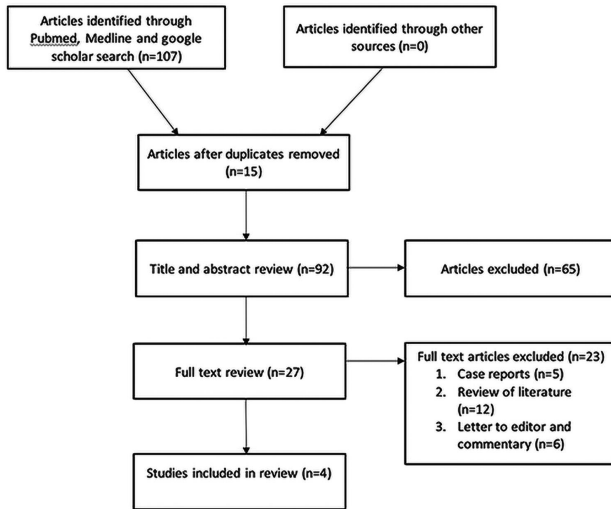


Fig. 1 Result of study selection with Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram.

Table 2 Characteristics of studies included in the review

S. no.	Article	Authors	Study design	Level of evidence	Number of patients	Outcome
1.	Cisternostomy: replacing the age old decompressive hemicraniectomy? ⁴	Iype Cherian Ghuo Yi Sunil Munakomi	Prospective nonrandomized controlled study (single person triple center)	3	DC = 284 DC + CS = 272 CT = 476	Mortality DC = 34.8% DC + CS = 26.4% CS = 15.6% GOS at 6 wk DC = 2.8 DC + CS = 3.7 CS = 3.9
2.	Role of cisternal drainage in patients with traumatic brain injury undergoing decompressive craniectomy ¹⁴	Amit Thapa Rupendra Bahadur Adhikari Bidur KC Bikram Shakya	Retrospective cohort study (double center)	3	DC = 73 DC + CS = 77	Mortality rate ($p = 0.052$) DC + CS = 28.6% DC = 43.8% GOS at 6 months ($p = 0.323$) DC + CS = 3.4 DC = 3.03
3.	Outcomes of severe head injury patients undergoing cisternostomy at tertiary care hospital in Nepal ¹⁶	Iype Cherian Hira Burhan	Retrospective case series	4	CS = 50	Mortality rate = 10% Good outcome at 2 months = 76%
4.	Implementation of cisternostomy as adjuvant to decompressive craniectomy for the management of severe brain trauma ¹⁵	Lorenzo Giammattei Daniele Starnoni Rodolfo Maduri	Retrospective cohort study	3	DC = 22 DC + CS = 18	Mortality rate DC = 27% DC + CS = 22% GOS >5 at 6 mo DC = 35% DC + CS = 61.1%

Abbreviations: CS, cisternostomy; CT, computed tomography; DC, decompressive craniectomy; GOS, Glasgow outcome scale.

cisternal pressure was lower than parenchymal pressure and the maintenance of the pressure gradient was associated with clinical improvement whereas rise in cisternal and parenchymal pressure and reversal of the gradient correlated with poor clinical outcome.¹²

CS as a surgical procedure in the setting of TBI was introduced for the first time in 2013 by Cherian et al.⁴ The principle of the procedure lies in drainage of CSF from basal cisterns, thereby equalizing the cisternal pressure to atmospheric level causing reversal of the pressure gradient created between cisterna and brain parenchyma, preventing the CSF shift edema and consequent rise in ICP.¹³ The classical surgical procedure in TBI, that is, decompressive craniectomy provides increased volume for the edematous brain to expand, but this novel procedure by influencing the basic mechanism of edema formation aims to limit the secondary injury. Even though this is an exciting development based on better understanding of the pathophysiology of the disease process, it would be prudent to examine the evidences examining its utility in TBI population.

The first prospective study evaluating CS in different cohorts of TBI patients was reported by Cherian et al.⁴ The author described his 6-year experience in his series on 1,032 patients overall, divided into three groups according to the procedure performed: decompressive craniectomy (DC) alone ($n = 284$), DC + CS ($n = 272$), and CS alone ($n = 476$). The population undergoing CS was heterogeneous consisting of 9.3% mild injury and 39.2% severe head injury. The outcome was described in terms of mortality in severe head injury group (34.8% for DC, 26.4% for DC + CS, 15.6% for CS alone), days on ventilator (CS = 2.4, DC + CS = 3.2, and DC = 6.3), and GOS at 6 weeks (DC = 2.8, DC + CS = 3.7, and CS = 3.9). CS was seen to confer a mortality advantage both in combination with DHC and as a standalone procedure compared with patient undergoing DHC alone. The patients in CS group also had decreased ventilatory requirement and higher mean GOS score at 6 weeks. However, there were several limitations in the study methodology and results. The demography and severity of injury in the study population as well as among the subgroup has not been commented upon. The methodology is also sparse on the management protocol being followed in head injury including the use of ICP monitoring and antiedema measures. The indications for carrying out surgical management and the rationale influencing the decision to opt for a particular surgical procedure is not clearly mentioned. Importantly, the intraoperative findings like severe brain edema, hematoma in peri-sylvian region, etc., which could impair the optimal visualization and opening of cisterns as well as their influence on the feasibility of procedure performed and intraoperative complications were not described. The postoperative complications and outcome stratified to the severity of injury were not adequately stated. The follow-up duration of 6 weeks also seem to be suboptimal for determining any definitive outcome for the study population. Even though it was a triple center study, all the procedures were performed by a single surgeon.

Thapa et al performed retrospective study comparing TBI patients who underwent DC ($n = 73$) with DC + CS ($n = 77$).¹⁴ The two groups were evenly matched except in terms of age (38.5 years in DC group vs. 31.7 years in DC + CS group $p = 0.016$) and GCS at presentation ($p = 0.034$). The procedure could be completed successfully in all the cases and it took an additional surgical time of 10 minutes. Death rate was 28.6% in DC + CS group compared with 43.8% in DC only group ($p = 0.052$) amounting to absolute risk reduction of 15.2% for DC + CS group. However, at 6-month follow-up, the mean GOS score between the two groups was not statistically significant (DC = 3.03 vs. DC + CS = 3.4, $p = 0.323$). As the groups were not evenly matched in terms of severity of injury (mean GCS at presentation) and mean age of patients, the demonstrated treatment effect could have been affected.

Giammattei et al performed a retrospective study in severe TBI patients comparing DC ($n = 22$) with DC + CS ($n = 18$).¹⁵ The groups were comparable with respect to age and GCS at presentation, but the DC + CS group had more patients with unilateral pupillary dilation (55 vs. 36%) and higher average Rotterdam CT score (4.7 vs. 3.8; $p = 0.03$). The decision to add CS to DC was based on the availability of surgeon skilled in vascular and skull base approaches, which can be a source of introducing selection bias. CS was successfully performed in all the 18 cases with slightly longer average operating time (204 vs. 178 minutes). Although the mortality rates were similar in both the groups (22 vs. 27%), the CS group had reduced mechanical ventilation duration, ICU stay, and also better GCS scores at the time of discharge ($p = 0.001$). At 6 months of follow-up, those patients in DC + CS group had more favorable clinical outcome (GOS ≥ 5 ; 61.1 vs. 35%; $p = 0.1$). Moreover, the patients in whom CS was performed as a primary procedure had better clinical outcome scores at 6-month follow-up ($p = 0.01$). However, the favorable results obtained in this study cannot be generalized because of retrospective nature of the study, limited number of patients and selection bias in choice of surgical procedure.¹³

Cherian and Burhan published yet another series exploring the role of CS as a standalone procedure in severe TBI patients.¹⁶ They recruited 50 severe TBI cases over 9 months duration. The patients with age more than 80 years and motor score of 2 and less were excluded, but those with bilaterally dilated pupil were included in the study. All the patient successfully underwent CS and bone flap was replaced in 48 out of 50 cases. The average cisternal drain pressure on first post-operative day was 9.3 mm H₂O which decreased to 7.0 mm H₂O on day 5. At 2-month follow-up, good recovery was seen in 76% cases, severe disability in 6 and 10% patients had died. Even though the results are promising, but the study lacks a control group.

Conclusion

Combined with DC has been shown to have favorable effect on mortality, duration of ventilator requirement and ICU stay, better GCS scores at discharge, and better clinical

outcome; CS as the standalone procedure has been shown to reduce cisternal pressure, along with conferring mortality benefit, reducing ventilator duration and ICU stay. The studies exploring this procedure have been limited by either sample size or study design even though the results have been promising but they need thorough and rigorous evaluation before it can be considered as standard of care either in adjuvant or standalone setting, therefore a well-designed multicentric randomized controlled trial is needed to critically examine utility and viability of the procedure in TBI patients.

Funding

None.

Conflict of Interest

None declared.

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