

External Lumbar Drainage for Refractory Intracranial Hypertension in Traumatic Brain Injury: A Systematic Review

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Research

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Abstract

Background

External lumbar drainage remains a controversial therapy for medically refractory intracranial hypertension in patients with acute TBI. This systematic review sought to compile the available evidence for the efficacy and safety of the use of lumbar drains for ICP control.

Methods

A systematic review of the literature was performed with the search and data extraction performed by two reviewers independently in duplicate.

Results

Nine independent studies were identified enrolling 230 patients, 159 with TBI. Efficacy for ICP control was observed across all studies, with immediate and sustained effect, reducing medical therapy requirements. Lumbar drainage with medical therapy appears effective when used alone and as an adjunct to ventricular drainage. Safety reporting varied in quality. Cerebral herniation (with unclear relationship to lumbar drainage) was observed in 14/230 patients resulting in one incident of morbidity without adverse patient outcome.

Conclusions

The available data is generally poor in quality and volume, but supportive of efficacy of lumbar drainage for ICP control. Few reports of adverse outcome are suggestive of, but are insufficient to confirm, safety of use in the appropriate patient and clinical setting. Further large prospective observational studies are required to generate sufficient support of an acceptable safety profile.

Introduction

Established management practices for moderate and severe traumatic brain injury (TBI) are centred on minimising secondary injury through normalising intracranial homeostasis. This is achieved through a therapeutic paradigm principally centred on the avoidance of raised intracranial pressure (ICP) and maintenance of cerebral perfusion pressure (CPP)[12]. Contemporary ICP management strategies utilise a sequential escalation of therapeutic intensity until ICP control is achieved, with protocols based on the Brain Trauma Foundation (BTF) guidelines[12]. Initial medical treatments for intracranial hypertension include: sedation, mild hypocapnia and hyperosmolar therapy. Where intracranial hypertension is refractory to these interventions, therapies including diversion of cerebrospinal fluid (CSF), barbiturate coma and decompressive craniectomy can be considered.

CSF diversion to manage raised ICP is classically understood in terms of the Monro-Kellie doctrine.[18, 25] The principle states that diversion (or buffering) of one constituent of the intracranial compartment (*i.e.* CSF) permits increasing volume of other constituents (*i.e.* parenchymal oedema in response to trauma). CSF can be removed from the system through two principle access points: (1) a ventriculostomy in the lateral ventricle connected to an external *ventricular* drain (EVD); or (2) a lumbar catheter connected to an external *lumbar* drain (ELD). CSF drainage can be achieved *intermittently* through discrete episodes of volume-controlled drainage, or *continuously* by permitting uninterrupted pressure-controlled drainage[30].

Traditionally, CSF diversion in TBI is achieved through a ventriculostomy. Siting a ventriculostomy also permits measurement of intraventricular pressure by transduction of a closed drain, though in recent years ICP monitoring has more commonly been achieved through intraparenchymal monitoring via a transcranial access device or “bolt”[7]. Practice varies from centre to centre, and between adults and paediatrics, with the usage of EVD monitoring and drainage being a more common practice in paediatric trauma centres[32], but less so in adults[16].

ELD originated in 1963 as a means for reducing cerebral tension intraoperatively[36], and has become an established method of CSF diversion in a variety of settings[8], including: post-traumatic CSF leak[5, 10], normal pressure hydrocephalus assessment[3], skull base surgery[33, 38], and in thoracoabdominal aortic surgery to reduce spinal cord ischaemia[15]. The use of ELD is traditionally considered controversial for use in patients suffering TBI. This is due to the potential risk of iatrogenic transtentorial

herniation, as demonstrated by historical examples of herniation after lumbar puncture in patients with raised ICP[14, 17, 23, 29]. In other contexts of intracranial hypertension, the use of ELD has been successfully adopted, including in bacterial and cryptococcal meningitis[2, 39] and subarachnoid haemorrhage (SAH)[27, 28, 34]; achieving similar ICP control to ventriculostomy drainage without significant complication rates.

Rationale:

Lumbar drainage represents a potential alternative means of CSF diversion to ventriculostomy due to avoidance of the passage of a drain through cerebral parenchyma. Insertion of a lumbar drain is a technically and logistically simpler procedure, particularly in patients with TBI whom often have small lateral ventricles rendering insertion of EVD challenging or not possible. Whilst thought to also achieve ICP control, concerns regarding the safety of lumbar drainage lie in the possible complication of cerebral herniation with associated morbidity and mortality. There is no systematic review of the evidence in the literature available to summarise the safety and efficacy of external lumbar drainage for ICP control in TBI.

Objectives:

Our objective is to systematically evaluate the available literature examining the use of external lumbar drainage of CSF for refractory intracranial hypertension in traumatic brain injury (TBI). Specifically, we seek to summarise the available evidence for: (1) the efficacy of the use of external lumbar drains in control of refractory intracranial hypertension in TBI; and (2) the safety of external lumbar drainage in acute TBI.

Methods

A systematic review of the literature was performed following the methodology of the Cochrane Handbook for Systematic Reviewers and presented in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) [24].

The primary review questions determined by the authors were:

- (1) Is CSF diversion via an external lumbar drain a safe procedure in TBI?
- (2) Does CSF diversion via an external lumbar drain effectively control intra cranial hypertension in TBI?

Secondary review questions determined by the authors were:

- (3) What selection/exclusion criteria are utilised for patient selection to determine appropriate candidates for external lumbar drainage?
- (4) Are there any established protocols for the use of external lumbar drainage for the control of ICP in TBI?

Inclusion Criteria:

Population:

The population of interest were human subjects with moderate or severe TBI, inclusive of both adult and paediatric populations.

Intervention:

The intervention considered is CSF diversion via an ELD.

Outcome measures:

The outcome measures of interest were ICP control, CPP optimisation and the safety profile of the intervention. A considered secondary outcome measure was any appropriate measure of functional outcome post-injury. Acceptable indices of ICP/ CPP control considered are: (1) direct measurement pre- and post- drainage and (2) indirect outcome measures of reduced incidence of

requiring osmotic therapy, hyperventilation, or more invasive surgical procedures (external ventricular drainage or decompressive craniectomy).

Setting:

Given the intensive monitoring required to gain the above data such studies would be in the intensive care unit or neurosciences critical care settings.

Methodology:

Any research methodology in humans was considered for inclusion, including observational studies and case series/reports.

Exclusion Criteria:

Studies conducted in animal models or *in vitro* human models were excluded. Studies which recorded the variables of interest, but did not report sufficient data on these variables for our research questions were also excluded.

Information Sources:

We systematically searched the following databases, from their respective inception to September 2020: Medline, Embase, Cochrane Central, NICE Evidence, Google Scholar and Web of Science. Reference lists of pertinent review articles on the topic were hand-searched for suitable articles. Reference lists of identified articles for inclusion were also hand-searched for suitable articles. See appendix 1 for an example search strategy.

Study Selection:

Studies were independently screened for inclusion by two reviewers, utilising a referential standardised proforma. Eligibility for study inclusion was defined as: a study of human patients with TBI, with the measurement of intracranial pressure via intraparenchymal or intraventricular pressure monitor, with insertion of an external lumbar drain for the purposes of CSF drainage with the therapeutic aim of ICP/ CPP control.

Data Extraction:

Data were extracted from included reports by two reviewers: conducted independently in duplicate, using piloted forms. Data extracted included; study characteristics, patient demographics, number of patients, ICP measurement method and frequency, external lumbar drainage timing and drainage protocol, patient selection/exclusion criteria, ICP/ CPP control outcome, avoidance of treatment intensity level escalation, functional outcome.

Risk of Bias in Individual Studies:

Two reviewers assessed the risk of bias of each individual study using the RTI item bank[35], with discrepancies discussed with a third party.

Synthesis of Results:

The heterogeneous nature of data collection and analysis methods precludes our ability to combine and synthesise results. As such a descriptive summary will be presented.

Results

Study Selection:

A search of the literature pertaining to lumbar drainage in TBI yielded 610 results. After the removal of duplicates, 453 research items were screened against the inclusion criteria. 27 full text items were retrieved for eligibility assessment, of which 12 studies were considered to fulfil the criteria (Figure 1).

Of the 12 research items eligible for inclusion[1, 6, 37, 9, 19–22, 26, 28, 34], all were published articles. Three of these articles included data presented in previously published articles: Munch et al., 2001 data were later published in Tuettenberg et al., 2009; Murad et al., 2008 data were later published in Murad et al., 2012; and Baldwin et al., 1991 data were later published in Levy et al., 1995. The most recent publications were included in the full qualitative synthesis; prior publications were not included to avoid duplicate reporting of data.

Study and Patient Demographics:

Three articles were presented as case series [1, 19, 22] with another presented as a case report and accompanying case series[37]. Five studies were presented as observational studies: three retrospective [9, 20, 21] and two prospective[28, 34]. Three studies utilised a mixed cohort of patients with TBI and aneurysmal subarachnoid haemorrhage (SAH) and/or intracerebral haemorrhage (ICH)[21, 28, 34] with six studies including only patients with TBI[1, 9, 19, 20, 22, 37]. One study included only paediatric patients [19], seven studies included only adult patients[1, 9, 20–22, 28, 37] and one included adults and children[34]. In total, 230 patients were included in the studies, of which 159 were patients with TBI. The demographics of included patients are reported in Table 1. Due to the manner in which the results were reported, the present authors were unable to delineate results pertaining only to TBI patients in the studies using a mixed cohort; as such the results will be presented together, noting where a mixed cohort is implicated where the results of these studies are discussed. Manet et al., 2016[22] and Manet et al, 2017[21] utilised a sub-cohort, including only patients with features of external hydrocephalus.

Whilst our exclusion criteria resulted in removal of studies which achieved CSF diversion through EVD alone, five of the nine studies included patients with an EVD in addition to ELD. In three studies, all participants had both EVD and ELD[19, 28, 37] with EVD preceding ELD, two studies had a mixed cohort of ELD with and without EVD[21, 34]. Llompert-Pou et al., 2011[20] included two patients (of 30) who received an EVD though it is not clear whether the insertion of EVD preceded that of ELD. Patients in the remaining studies had ELD alone, with patients included in Manet et al, 2016[22] only receiving ELD where EVD insertion had failed or was contraindicated.

Eight studies only included patients with either: no surgical intracranial lesion or a surgical intracranial lesion post-evacuation; in one study this was not specified[1]. All study protocols only instigated CSF diversion where medical management options had failed, all specifying at least hyperventilation and osmotic therapy in their ICP management protocols. Six studies indicated use of barbiturate coma[1, 19, 20, 22, 34, 37] and five indicated use of hypothermia[1, 20–22, 37]. Four studies indicated use of ventricular drainage prior to ELD[21, 28, 34, 37] where possible.

Efficacy:

All studies reported a marked reduction in ICP after CSF diversion with an ELD. Individual study results are reported in Table 2. The three studies[9, 20, 34] reporting outcome of statistical tests of this effect all reported statistically significant reduction in ICP after introduction of lumbar drainage. Of four studies[1, 19, 28, 34] presenting data or observations on the effect of lumbar drainage on CPP, all reported a positive effect. Four studies presented observations on the effect of lumbar drainage on treatment intensity or requirement for other ICP lowering therapies[1, 21, 28, 34]. All four reported a beneficial effect on the requirement of other therapies after institution of lumbar drainage.

Safety

Of 230 patients, there were 14 reports of either radiological or clinical signs of cerebral herniation after insertion of ELD (Table 3). One study[34] reported 12 of the 14 incidences of cerebral herniation, but the relationship between development of clinical/radiological signs of cerebral herniation and the introduction of lumbar drainage is not described. One of these episodes was reported as occurring due to the iatrogenic disconnection and uncontrolled drainage from the lumbar drain, and the patient survived without neurological deficit. In the eight patients of these 12 who subsequently died, the authors did not attribute any death to, or as a complication of lumbar drainage. There were two further incidences of herniation reported in the included literature, one patient exhibited only radiological signs[9] (bilateral uncal herniation), and one patient developed a fixed dilated pupil four hours after insertion of ELD which returned to normal after surgery and the patient made a “good neurological recovery”[28].

There were 9 reported incidences of central nervous system (CNS) infection in the included studies. A further six patients had a positive cerebrospinal fluid culture sample which was treated as contaminant. 7/9 CNS infection cases were reported to have both EVD and ELD in situ. There were 20 incidences of lumbar drain failure requiring revision. Eleven patients were reported to require long term CSF diversion with insertion of a CSF shunt.

Eight studies reported functional outcomes [1, 9, 19–22, 34, 37], and one reported mortality alone[28]. No study explicitly reported a case whereby a complication from use of lumbar drain contributed to mortality or poor neurological outcome.

CT criteria

Seven of the nine studies stipulated requirement of a CT head prior to proceeding with insertion of an ELD[1, 9, 20–22, 34, 37]. Two studies required this in the preceding 24 hours[1, 20], and one in the preceding 8 hours[9]. All studies requiring CT described imaging criteria[1, 9, 20–22, 34, 37], all including discernible basal cisterns and absence of a surgical mass/cerebral herniation. Three studies also included the requirement of midline shift of < 10mm [1, 20, 21]. Manet et al, 2017[21] used the presence of “a gradual development of subdural or subarachnoid collections located in the sylvian and/or interhemispheric fissures and/or cortical sulci” as evidence of external hydrocephalus and thus inclusion in their study. Bauer et al., 2017[9] proposed and utilised a scoring system based on the patency of the prepontine and quadrigeminal cisterns, and absence of uncal and foraminal herniation on the pre-procedural imaging.

ELD drainage protocol

Eight studies utilised an ELD in all patients [1, 19–22, 28, 34, 37]. One study used a single lumbar puncture or intermittently open drainage in four of nine patients[9]. Of the eight studies which utilised only ELD, six used protocols with a continuous drainage strategy[1, 19–22, 34]. One study[28] used varying methods, either continuous pressure controlled drainage or fixed drainage at 10 ml/hr. One did not state their drainage protocol[37]. Four studies describe an initial high drainage protocol until ICP control was achieved, with intensive pupillary examination[19, 21, 22, 34], two of which were in external hydrocephalus. Further details of specific drainage protocols are available in Appendix 2.

Risk of bias assessment

Due to the observational design of the included studies, risk of bias was deemed low to moderate in all studies. The risk of bias where considered moderate was on the basis of poor intervention detail or outcome reporting.

Discussion

The aim of this systematic review was to evaluate the available efficacy and safety data regarding the use of lumbar drainage for ICP control in TBI. The literature identified represents a small evidence base supporting the efficacy of lumbar drainage, where 9 independent studies observed the effects in 159 patients with TBI (230 patients overall). Other than infection, need for drain revision and transient mydriasis, one incident of morbidity (not affecting neurological outcome) was reported in these studies; though this is suggestive of safety of ELD in TBI, the small cohort is insufficient to conclusively confirm it.

Efficacy:

The data presented in the included studies supports the efficacy of lumbar drainage for ICP control as an adjunct to best medical therapy where optimal medical management has failed. Every study reported a beneficial effect for ICP control overall, with all of those performing statistical analysis finding a significant reduction in ICP following ELD insertion. Studies reporting mean reduction values utilised data one hour before and after commencing lumbar drainage, which unanimously confirmed an immediate effect. The positive effects on reducing need for medical interventions such as osmotic therapy are also encouraging, and were observed in all four studies reporting this outcome. The effect has been observed, though only reported for small numbers of patients, with increasing efficacy up to three days after instigation of lumbar drainage[1]. Together with one hour pre- and post-ELD ICP readings, the effect of lumbar drainage appears to be both immediate and sustained.

A significant reduction in ICP was reported in four studies which included ventriculostomy drainage prior to lumbar drainage[21, 28, 34, 37], suggesting that ELD offers both a benefit when used as the sole modality of CSF diversion, and additional benefit when used in combination with EVD.

Functional outcomes were not considered as a marker of “efficacy”, rather ICP control can be considered as a surrogate marker of potentially improving functional outcome due to the association of intracranial hypertension and poor outcome[4]. The numbers enrolled in these combined studies are by far insufficiently powered to assess for an effect on functional outcome.

Safety:

The available data identified by this systematic review is insufficient to draw firm conclusions on the safety profile of ELD in management of raised ICP in TBI, however the included studies here have not reported incidents of the usage of ELD directly contributing to mortality. A single case of ELD usage has been reported to result in pupillary changes requiring urgent surgery with good neurological recovery). However, the absence of significant complications in a series of 159 patients with TBI is unlikely to generate sufficient confidence to assuage the reservations held by some neurosurgical centres. In the single reported case of cerebral herniation requiring surgery, this was urgently recognised and appropriately managed resulting in good neurological recovery. Despite historical concerns of “coning” from lumbar puncture or drainage, the results suggest that in the modern intensive care unit, there is sufficient clinical monitoring to facilitate early recognition of cerebral herniation through clinical and radiological assessment and prompt remedial action.

Whilst a high mortality rate is not justification for therapeutics with the potential for harm, the alternative to lumbar drain is typically insertion of EVD or decompressive craniectomy, neither of which can be considered to be low morbidity. Whilst not robust, the results here are suggestive of a low to very low risk of severe morbidity or mortality as a result of ELD. When considering surgical risk, ELD offers the potential benefit of achieving ICP control without the need for decompressive craniectomy.

Infection rates of the included studies were 3.9%, though some incidences of infection were in patients with both EVD and ELD. This incidence is similar to that reported in the literature, with infection rates of ELD reported as 4.2-7%[13, 31] and EVD reported as 7-9%[11, 31].

CT criteria:

Given the concern of obliterated basal cisterns preventing CSF movement across the foramen magnum, considered patient selection would be a necessary component of implementing lumbar drainage. Patient selection on the basis of radiological criteria was common to most of the included studies. A number of the included studies refer to the protocol in Munch et al, 2001 to cite the earliest example, though Willemse et al 1998 include a similar protocol: discernible basal cisterns and absence of surgical mass lesions. Absence of tonsillar herniation, midline shift of less than 10 mm, and patency of prepontine and interpeduncular cisterns have been more recent additions. Due to the low complication rate, it would be difficult to identify which protocol is the optimal for safety in patient selection. Further details of the radiological features of those with transient mydriasis are not available to make a post-hoc assessment of which further features transpired to be associated with risk.

Drainage strategies:

Drainage strategies varied amongst studies, with insufficient data reporting to draw conclusions regarding the optimal protocol. The protocols where described adopt broadly similar strategies: greater drainage permitted to achieve ICP control (<20 mmHg), with subsequent “maintenance” drainage (ICP in the region of 10-20 mmHg) and closure of the drain where ICP was low (<10 mmHg). Pressure settings of the ELD varied widely between 0 cm above the foramen of Monro (FOM) and 20 cm above. The study reporting a fixed dilated pupil four hours after ELD insertion allowed free drainage at 0 cm[28]; a strategy which physiologically would permit continued drainage in the context of early cerebral herniation. Similarly, Tuettenberg et al., observing 12 episodes of unilateral mydriasis in their mixed TBI/SAH cohort, permitted free drainage at 5 cm above the FOM. Differing strategies for drainage should also consider nursing practicalities: continuous drainage at lower pressure settings is more likely to result in high volume outputs between nursing monitoring intervals.

When considering physical and biomechanical aspects of drainage, a minimum volume is required to produce an acceptable ICP/ CPP for the purpose of optimising perfusion and minimising the requirement for intervention. Therefore a sliding scale hourly drainage target, with an arbitrary maximum per hour of 10 ml may provide an attractive safe starting point in the views of the authors. Physically the volume of any potentially herniated neuro-axial tissue cannot exceed that of the volume of fluid drained, supporting further the likely safety of small incremental drainage as opposed to open pressure regulated drainage where theoretically no limit on the volume of drained fluid or herniating tissue exists.

Concomitant EVD:

As outlined above, ELD appears to offer additional benefit when used as an adjunct to EVD in ICP control. In the largest included study[34] 84/100 patients had received ventricular drainage prior to ELD which had failed to control their ICP, though it is not specified in the methods whether ventricular drainage continued once ELD was inserted. Given that the concerns surrounding lumbar drainage are centred on a pressure gradient across the foramen magnum, simultaneous EVD and ELD drainage theoretically reduces the risk of this occurring. However, this study reported a relatively high rate of signs of cerebral herniation (with unclear timing in relation to ELD).

ELD or EVD:

The prospect of utilising ELD instead of, or as an adjunct to, EVD in selected patients has some potential benefits. The procedure itself can usually be achieved more quickly, without need for transfer to an operating theatre. As observed by Manet et al[22], lumbar drainage also presents an opportunity for CSF diversion in a subset of patients for whom insertion of EVD is contraindicated or where insertion has failed. The prevalence of "slit" ventricles in the TBI cohort with intracranial hypertension presents a further technical challenge. As described above, ELD appears to be beneficial for ICP control where ventricular drainage has been established.

Limitations:

The limitations of the present study are primarily due to the heterogeneity of both the included studies and the data which they have presented. Exclusion of studies with a mixed cohort of brain injury aetiology and adult/paediatric cohort would have further narrowed the low patient and study numbers available for consideration by this study. As such we have included these, particularly given the necessity to be comprehensive when considering the intervention's safety profile. Further to this, even with these inclusions, the numbers of patients and studies are low, though identifying paucity in the literature serves as an outcome of this review. The detail in reporting of potential complication events was variable but generally poor. This is in part likely to be related to the incidence of clinical and radiological evidence of "coning" being a potential part of the natural history of severe TBI with refractory intracranial hypertension. As such we have only considered complications to be related to lumbar drainage where the respective authors have themselves reported these events to be as a consequence of lumbar drainage. Given the heterogeneity of cohorts and data reporting, it was not deemed suitable nor beneficial to perform a meta-analysis and a narrative review of the data is inherently limited in the conclusions which it may draw.

Implications:

Whilst this data cannot confirm a safety profile, this review confirms efficacy of ELD in ICP control. There remains equipoise regarding the use of ELD or EVD in the management of medically refractory intracranial hypertension in trauma. The authors advocate further large-scale multi-centre prospective observational studies to gain sufficient data to explore the safety of ELD in this context.

Conclusion

The literature appears to support the efficacy of lumbar drainage in ICP control where medical management has failed, though the data on its safety is encouraging but insufficient to draw conclusive recommendations. The efficacy and safety profile of ELD in comparison to EVD is not known, though ELD appears to be beneficial for ICP control both alone and where EVD has failed. Although the evidence base is insufficient to draw firm conclusions, based on the available evidence there is no clear indication that the complication rates of ELD are greater than those of EVD. Further large prospective observational studies are required to

generate sufficient support of an acceptable safety profile, with the possibility of subsequent randomised controlled studies to ultimately assess therapeutic parity.

Declarations

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None to declare.

Competing interests:

The authors declare that there is no conflict of interest.

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Available on request

Code availability:

N/A

Authors' contributions:

All authors contributed substantially to the work. All authors were responsible for concept and approved the manuscript. AS, WC, YC and ET performed the literature search, data extraction and risk of bias assessments. DD and AB provided critical support and oversight. AS drafted the final manuscript, critically revised by WC, YC, ET and DD.

Ethics approval:

N/A

Consent to participate

Not applicable

Consent for publication

Not applicable

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Tables

Table 1. Characteristics of patients in included studies.

Authors	Cohort	n =	TBI n	Other n	Mean initial GCS	Mean age	Gender F:M	Inclusion Criteria	Exclusion Criteria
Abadal Centellas et al, 2007	Adults, TBI	17	17	0	8	32.5 ± 13.3	4:13	Refractory ICP after first and second level measures	CT criteria
Bauer et al, 2017	Adults, TBI	8	8	0	10.1*	54.1 (27-70)	2:6	Refractory ICP with either small ventricles or high ICP disproportionate to CT	CT criteria
Levy et al, 1995	Children, TBI	16	16	0	6.2	Not stated	5:11	Considered if sustained ICP >25 on aggressive medical therapy	Nil stated
Llompart Pou et al, 2011	Adults, TBI	30	30	0	9	34.9±12.5	5:25	Refractory ICP after first and second level measures	CT criteria
Manet et al, 2016	Adults, TBI (EH)	4	4	0	10	53.5±7	2:2	Failure of maximal medical management and not suitable for or failed EVD, with increasing volume of CSF in SAS paradoxical to ICHT	CT criteria, no mass lesion or CT factors indicating craniotomy or decompressive craniectomy
Manet et al, 2017	Adults, TBI/SAH/ICH (EH)	33	22	11 (SAH n=10, ICH n=1)	7.9	51 (median) (34-61)	Not available	External hydrocephalus from acute brain injury, refractory ICP with radiological evidence of external hydrocephalus	CT criteria
Murad et al, 2012	Adults, TBI/SAH	15	10	5 (SAH)	6.8	36.9 (19-60)	3:12	Aged 18-99 with ventriculostomy catheter, ICP >20mmHg no longer responsive to medical criteria	Unevacuated focal mass lesion, patients transferred with lumbar drains
Tuettenberg et al, 2009	Adults, TBI/SAH	100	45	55 (SAH)	7±4 (TBI 6.4±3)	43.7 (TBI 37.6±18.1)	Not available	Ongoing ICP >20, EVD in situ, CT parameters and acceptable clotting	Nil stated
Willemse, 1998	Adults	7	7	0	6	26 (21-35)	3:4	Lumbar drainage was only instituted in the absence of focal mass lesions and with discernible basilar cisterns on	Nil stated

TOTAL 230 159 71

*excluding missing data for one patient with unknown initial GCS, TBI = traumatic brain injury, SAH = subarachnoid haemorrhage, ICH = intracerebral haemorrhage, EH = external hydrocephalus, GCS = Glasgow coma scale, EVD = external ventricular drain, ICP = intracranial pressure, CT = computed tomography.

Table 2. Efficacy measures of ELD reported by included studies.

Authors	Cohort	EVD?	ELD volume drained	Effect on ICP	CPP control outcomes	Prevention of TIL escalation?
Abadal Centellas et al., 2007	n =17 (adults, TBI)	No	Initial drainage of CSF to low ICP as described was 8.0 +/- 5.7 mL.	Mean ICP before and 1 hour after placement of ELD was 30.9 +/- 7.9 and 14.1 +/- 5.9 mm Hg. Excellent/good control of ICP achieved in 76% by day 1 and 94% by day 3.	Improvement in CPP in all patients.	Excellent control of ICP (no mannitol or hypertonic saline used over 24hr period) in 94% day 3 post ELD
Bauer et al., 2017	n = 8 (adults, TBI)	No	23.5 ml/24 h (mean, SD 16.41, range 0–40 ml)	Lumbar CSF removal led to a reduction of ICP in all patients Mean ICP was 22.3 mmHg (SD 3.0) before CSF drainage and was 13.9 mmHg (SD 4.7) after drainage (P = 0.002).	Not documented	Not reported
Levy et al., 1995	n=16 (children, TBI)	Yes in all	Not stated	14 of the 16 children had an abrupt and lasting decrease in ICP after placement of the lumbar drain, which obviated the need for continued aggressive medical therapy	CPP improved in one case, otherwise not documented.	Not reported
Llompart Pou et al., 2011	n=30 (adults, TBI)	No	Not stated	ICP before and one hour after ELD placement was 33.7±9.0 and 12.5±4.8 mmHg respectively, a decrease in ICP of 21.2±8.3 mmHg (P <0.0001)	Not documented	Not reported
Manet et al., 2016	n= 4 (adults, TBI, EH)	No	Not stated	This procedure resulted in the immediate and long-lasting control of ICP	Not documented	Not reported
Manet et al., 2017	n=33 (adults, TBI/SAH/ICH, EH)	Mixed (8 of 33)	Median CSF flow was 119 ml (96–280) per day	The ELD procedure led to a marked averaged reduction of ICP over the following 6 h by 16 mmHg (13–24), from 25 mmHg (20–31) before to 7 mmHg (3–10) after ELD	Not documented	Sedation was reduced in 25 patients (75%) within the 24 h after ELD insertion.
Murad et al., 2012	n=15 (adults, TBI/SAH)	Yes in all	Not stated	Reduced from mean of 28.2 mm Hg +/- 6.5 to 10.1 +/- 7.1	CPP increased from 76.7 mmHg +/- 19.8 to 81.2 +/-10.2	Reduced patients requiring boluses of osmotic therapy from 12/15 to 1/15.
Tuettenberg et al., 2009	n=100 (adults, TBI/SAH)	Mixed (84 of 100)	Not stated	Significant reduction in ICP from 32.7 ± 10.9 to 13.4 ± 5.9 mm Hg (p < 0.05)	Increase in CPP from 70.6 ± 18.2 to 86.2 ± 15.4 mm Hg (p < 0.05).	All modalities reduced except hyperventilation
Willemse, 1998	n = 7 (adults, TBI)	Yes in all	Not stated	Five of the seven patients had a lasting decrease in ICP after lumbar drainage and survived.	Not documented	N/A

TBI = traumatic brain injury, SAH = subarachnoid haemorrhage, ICH = intracerebral haemorrhage, EH = external hydrocephalus, GCS = Glasgow coma scale, EVD = external ventricular drain, ICP = intracranial pressure, CT = computed tomography

Table 3. Adverse events and complications reported in included studies.

Authors	Cohort	EVD?	CSF infections	LD revisions	Number requiring a shunt	Cerebral herniation post-ELD?	Details
Abadal Centellas et al., 2007	n = 17 (adults, TBI)	No	0 (3 contaminants)	2 (5 blockages)	0	n = 0	No pupil changes in 24 hours post insertion
Bauer et al., 2017	n = 8 (adults, TBI)	No	None stated	None stated	None stated	n = 1	One patient showed an uncal herniation on both sides after lumbar CSF withdrawal without mydriasis or other clinical signs of cerebral herniation
Levy et al., 1995	n = 16 (children, TBI)	Yes in all	None stated	None stated	3	n = 0	Two patients had fixed and dilated pupils prior to ELD insertion, remained so after lumbar drainage commenced.
Llompert Pou et al., 2011	n = 30 (adults, TBI)	No	1 (4 with positive cultures, 3 contaminant)	4 (8 obstruction)	3	n = 0	No pupil changes in 48 hours post insertion
Manet et al., 2016	n = 4 (adults, TBI)	No	0	0	0	n = 0	N/A
Manet et al., 2017	n = 33 (adults, TBI/SAH/ICH)	Mixed (8/33)	1	0	5	n = 0	N/A
Murad et al., 2012	n = 15 (adults, TBI/SAH)	Yes in all	0	None stated	None stated	n = 1	Fixed dilated pupil four hours after ELD insertion, which returned to normal after surgery hours
Tuettenberg et al., 2009	n = 100 (adults, TBI/SAH)	Mixed (84/100)	7 (all also had EVD)	14/100	None stated	n = 12	No relationship to ELD described. All had unilateral mydriasis. 4/12 survived. Three patients died from cerebral herniation secondary to intracranial hypertension, three had devastating injury prior to ELD, one died from pulmonary embolism, one died from cerebral infarction. No reports of morbidity or mortality directly from ELD.
Willemse, 1998	n = 7 (adults, TBI)	Yes in all	None stated	None stated	None stated	n = 0	N/A

TBI = traumatic brain injury, SAH = subarachnoid haemorrhage, ICH = intracerebral haemorrhage, EH = external hydrocephalus, GCS = Glasgow coma scale, EVD = external ventricular drain, ICP = intracranial pressure, CT = computed tomography

Figures

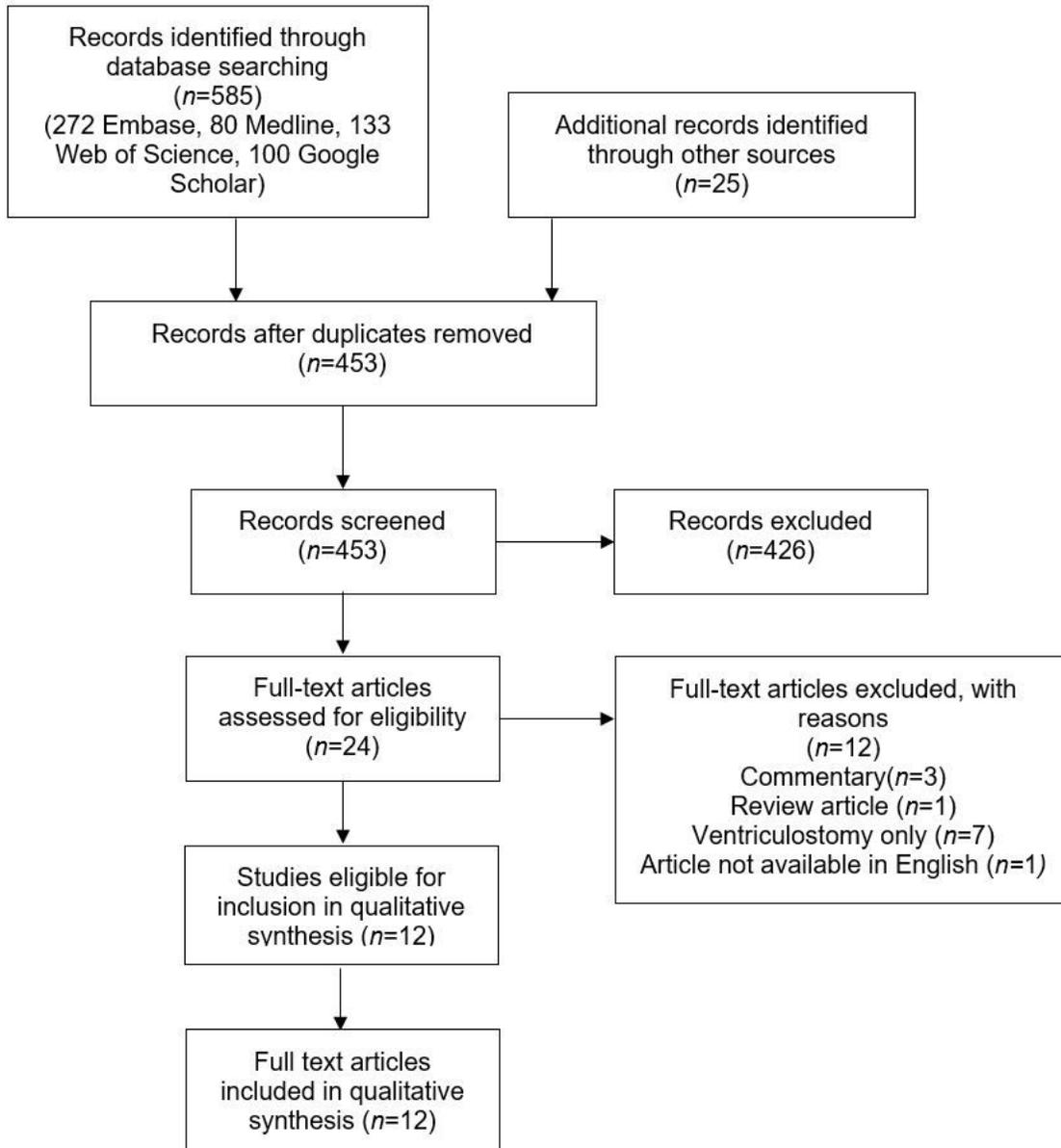


Figure 1

Search results