

External lumbar drainage for the management of refractory intracranial hypertension in pediatric severe traumatic brain injury: a retrospective single-center case series

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OBJECTIVE Guidelines for the management of pediatric severe traumatic brain injury (TBI) recommend external ventricular drainage for CSF drainage as a first-tier treatment in the intracranial pressure (ICP) pathway. However, ventriculostomy in children can sometimes be challenging because of the small size of the lateral ventricles. External lumbar drainage (ELD) may be a useful alternative; therefore, the authors analyzed the outcome of a cohort of pediatric patients who underwent ELD to manage intracranial hypertension (ICH).

METHODS This study retrospectively enrolled pediatric patients with ICH following severe TBI who underwent ELD. Radiological and clinical severity scores (Marshall classification, Rotterdam score, Injury Severity Score, and Pediatric Trauma Score) were noted. ICP and cerebral perfusion pressure (CPP) curves were analyzed 12 hours before and after the procedure. Any change in medical therapy was recorded, as well as the total volume and duration of drainage. Cerebellar tonsillar position according to the McRae line was noted before and after ELD. Glasgow Outcome Scale-Extended score at follow-up was also noted.

RESULTS Thirty patients were included, with a mean age of 8 ± 4.4 years, and a median admission Glasgow Coma Scale score of 7 ± 4 (range 3–13). ELD was performed after a median delay of 1 day (range 0–7 days), mean drainage volume/day was 296 ± 129 ml, and median duration of drainage was 7 ± 5 (range 2–12) days. Forty-three percent of the patients underwent ELD as a part of the first-tier therapy. ICP decreased after ELD (mean difference 13.4 ± 6.2 mm Hg, $p < 0.001$), whereas CPP increased (mean difference 10.6 ± 6.4 mm Hg, $p < 0.001$). Fifty-three percent of the cohort did not need any further second-tier therapy after ELD. The study found 1 case of drain revision and 3 cases of cerebellar tonsil herniation.

CONCLUSIONS These preliminary data suggest ELD is a valuable option to treat ICH in severely head-injured children, limiting the use of second-tier treatments. This pilot study should lay the foundation for a multicenter prospective trial.

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KEYWORDS external lumbar drainage; ELD; intracranial hypertension; ICH; case series; pediatric TBI; traumatic brain injury

THE 2019 third edition of the Guidelines for the Management of Pediatric Severe Traumatic Brain Injury¹ (TBI) and the associated algorithm provided by the guidelines committee² recommended CSF drainage

as a first-tier treatment in the intracranial pressure (ICP) pathway, after baseline care. A class III.1 recommendation endorsed the use of external ventricular drainage (EVD) to control ICP after TBI. In clinical practice, however, the

ABBREVIATIONS BTF = Brain Trauma Foundation; CPP = cerebral perfusion pressure; DC = decompressive craniectomy; ELD = external lumbar drainage; EVD = external ventricular drainage; GCS = Glasgow Coma Scale; GOS-E = Glasgow Outcome Scale-Extended; ICH = intracranial hypertension; ICP = intracranial pressure; IQR = interquartile range; ISS = Injury Severity Score; MVC = motor vehicle collision; PaCO₂ = partial pressure of CO₂; PTS = Pediatric Trauma Score; SAH = subarachnoid hemorrhage; TBI = traumatic brain injury.

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frequent occurrence of slit ventricles in children can make external ventricular drain placement technically challenging and only temporarily effective in CSF drainage. In a large series of 96 children, Jagannathan et al. investigated the management of posttraumatic intracranial hypertension (ICH) and found that EVD was deemed feasible in 24% of patients, with satisfactory ICP control in 85% of cases.³ Furthermore, the two main series investigating the efficacy of EVD in pediatric TBI reported a rate of EVD-related meningitis of 8.3% and 22%, respectively, in pediatric TBI series.^{3,4}

External lumbar drainage (ELD) represents an attractive alternative, as it is a simple bedside procedure to drain the high-volume spinal subarachnoid compartment, with a low rate of infectious complications. Its role in TBI has not gained popularity over the years, notably because of the potential risk of tonsillar herniation. Recently, a systematic review of 9 studies and 230 patients (including 16 children) who underwent ELD for ICH showed high efficacy in controlling ICP, along with a low complication rate (infection 3.9%, clinical or radiological evidence of cerebellar herniation 6%).⁵

In pediatric TBI, there are only two published pediatric series about ELD and both are from the same team (Barrow Neurological Institute).^{6,7} Baldwin et al.⁶ reported 5 children who underwent ELD after EVD failure under maximal medical therapy (including burst suppression), while Levy et al.⁷ presented a larger series (16 children, including the 5 cases previously published) treated with the same protocol (ELD after failure of EVD) but at various timings (5 patients in a barbiturate coma, 6 receiving intermittent barbiturates, 5 patients not receiving barbiturates). Except for 2 children who died from massive diffuse brain swelling, the authors obtained satisfactory ICP control in most (14 of 16) of the patients.

Based on these data, the latest edition of the Brain Trauma Foundation (BTF) pediatric guidelines deem the level of evidence supporting the use of ELD insufficient, thus ELD is currently not recommended in posttraumatic ICH management.¹ We therefore analyzed our cohort of pediatric patients with severe TBI with the aim of 1) investigating the safety of this procedure, 2) studying the efficacy of ELD in the management of ICH, and 3) evaluating the importance of ELD timing on patient outcome.

Methods

Study Design and Data Extraction

This retrospective single-center case series included consecutive children < 18 years old with TBI who underwent ELD to control ICH between 2010 and 2022 at Hôpital Necker-Enfant Malades in Paris, France, a pediatric level 1 trauma center. Exhaustive data extraction from our institution's electronic files was performed using our search engine software (Dr. Warehouse).⁸ Patients were excluded in cases of concomitant skull base fracture requiring the placement of an external lumbar drain to prevent or treat a CSF leak. This case series is reported consistent with the guidelines of Preferred Reporting of

Case Series in Surgery (PROCESS) guidelines.⁹ Ethical approval was granted by Commission Nationale Informatique & Libertés (CNIL).

Management of ICH

Severe TBI was managed according to the recommendations of the French Society of Anesthesia and Intensive Care¹⁰ and the BTF pediatric guidelines.² Pediatric patients with TBI and Glasgow Coma Scale (GCS) scores < 8 underwent clinical evaluation by the trauma team,¹¹ initial resuscitation, and then a whole body CT scan. Intracranial ICP monitoring was performed in the following cases: 1) abnormalities detected on the brain CT scan, or 2) a patient needing prolonged intubation for concomitant systemic injury. Transcranial Doppler ultrasonography was performed at admission and regularly during hospitalization.¹²

Medical management consisted of optimization of ventilation (partial pressure of CO₂ [PaCO₂] targeted to 35 mm Hg with normoxia), osmotic therapy, adequate sedation, and/or the introduction of neuromuscular blockades. In cases of refractory ICH (i.e., sustained ICP elevation > 20 mm Hg for more than 5 minutes, despite optimal medical treatment), second-tier treatments were introduced. Patients underwent burst-suppression therapy (thiopental, maximum dosage 5 mg/kg/hr). Cerebral perfusion pressure (CPP) was maintained above 40–45 mm Hg for younger children and above 50–55 mm Hg in children older than 2 years. Decompressive craniectomy (DC) was proposed in children with persisting ICH despite maximal medical therapy.

ELD was considered in patients with refractory ICH if they were not candidates for mass evacuation surgery or EVD (virtual slit ventricles), and had discernible cisterns (compressed cisterns were accepted); it was contraindicated in cases of tonsillar herniation on cranial CT.¹³ The indication and timing were discussed by the neurosurgeon and the neurointensivist in one of the following scenarios: 1) after osmotic diuretics and/or optimization of sedation; 2) after the induction of a barbiturate coma; or 3) after surgery for space-occupying lesions and primary DC. If the indication of ELD was retained, a head CT scan or MRI was repeated to confirm the absence of a contraindication.

ELD was performed bedside, in a sterile setting, using a silicone catheter introduced in the subdural lumbar space (Lumbar Catheter Accessory Kit, Integra LifeSciences) with a 16G Tuohy needle, tunneled for approximately 10 cm at the level of the patient's side and connected to a collecting pouch (hermetic external CSF drainage, Integra LifeSciences). The drainage system was placed between 5 and 10 cm H₂O above the level of the tragus and continued until achieving sustained normal ICP (< 20 mm Hg). The volume of drainage was also monitored every 3 hours: the level of ELD was promptly adapted in cases of rapid increase. In cases of refractory ICH despite ELD, treatment was further escalated; no change in ELD level was attempted, to prevent the risk of cerebellar herniation. Control imaging was performed systematically after approximately 7 days of drainage or in cases of clinical or hemodynamic unexpected changes. The external lumbar

TABLE 1. Radiological and clinical indices of trauma severity

Index	Whole Cohort	Group 1, n = 13	Group 2, n = 17	p Value
Marshall classification, n (%)				0.6
Diffuse injury II	10 (33)	6 (46)	4 (23)	
Diffuse injury III	14 (47)	4 (31)	10 (59)	
Diffuse injury IV	5 (17)	2 (15)	3 (18)	
NEML	1 (3)	1 (8)		
Median Rotterdam score (range)	3 (1–5)	3 (2–5)	4 (1–5)	0.4
Median PTS (range)	6 (2–10)	6 (3–10)	6 (2–8)	0.8
Median ISS (range)	20 (4–41)	18 (4–41)	21.5 (4–34)	0.15

NEML = nonevacuated mass lesion.

No significant difference was found among patients undergoing ELD as a part of the first-tier therapy (group 1) and those who underwent ELD after the failure of the second-tier therapy (group 2).

drain was removed after discussion with the neurointensivist when the patient was planned to be extubated or in instances of radiological and/or clinical evidence of cerebellar herniation.

Trauma Evaluation and Outcome Measures

Mechanism of injury, GCS score before orotracheal intubation, Pediatric Trauma Score (PTS), and Injury Severity Score (ISS) were noted. Marshall classification and Rotterdam score were calculated on CT scans to quantify the severity of brain injury.^{14,15} We also reported the mortality rate, length of tracheal intubation, and Glasgow Outcome Scale-Extended (GOS-E) score at last follow-up. Favorable outcome was defined as a GOS-E score between 5 and 8 at last follow-up. Three ELD outcome measures were analyzed.

Safety of ELD

Most reported complications after ELD are infections, system revisions, and tonsillar herniations.⁵ We determined the effect of drainage on tonsillar position as the difference of the distance of the tip of the tonsil and the McRae line on a midline sagittal image between the initial cranial CT scan and the follow-up MRI after ELD removal. Tonsillar herniation was defined as a ptosis > 5 mm from the McRae line. Bauer et al.¹⁶ proposed a score to assess the safety of lumbar drainage by analyzing the discernibility of prepontine and quadrigeminal cisterns and evidence of uncal and foramenial herniation (ELD safe for a score \geq 5). This score could be helpful for the evaluation of ICP changes during drainage, thus we retrospectively analyzed it in our cohort.

Efficacy of ELD to Control ICH

ICP and CPP values were noted every hour between –12 and 12 hours after ELD placement. Furthermore, we studied the impact of ELD placement on treatment escalation as the proportion of patients who achieved sustained normal ICP values with no further need of second-tier treatment for the management of ICH; in patients under barbiturate coma, this meant a decrease in thiopental dose within the first 24 hours after ELD placement.

Impact of Timing of ELD on Outcome

A subgroup analysis was performed to evaluate the differences in ELD efficacy between patients treated during the first- (group 1) and second-tier therapy (group 2).

Statistical Analysis

Descriptive statistics were performed to analyze cohort survival and compare the management strategies, reported as mean \pm standard deviation or median \pm interquartile range (IQR). The mean values of ICP and CPP before and after ELD were compared using a Student t-test for independent samples. A linear logistic regression model was built to analyze the evolution of ICP and CPP over time. Statistical analysis was performed using SPSS Statistics (version 24.0, IBM Corp.).

Results

Cohort

Thirty patients were enrolled, with a male/female ratio of 1.6:1, and a mean age of 8 ± 4.4 (range 1–16) years. Motor vehicle collision (MVC) was the most common cause of TBI (16 patients, 53%), followed by defenestration (11 patients, 37%). The median GCS score at admission was 7 ± 4 (range 3–13), the median ISS was 20 (range 4–41), and the median PTS was 6 (range 2–10). Most of the patients had a Marshall diffuse injury III (14 cases, 47%) followed by diffuse injury II (10 patients, 33%). The median Rotterdam score was 3 (range 1–5) with almost half of the patients with higher scores (range 4–6, 48.6%; Table 1). The median follow-up was 20 (range 0.23–123) months.

Timing of Procedure

ELD was placed with a median delay of 1 day after admission (range 0–7 days). In almost half of the cases, the procedure was performed as part of the first-tier therapy of ICH (group 1, 13 patients), after additional sedation (3 patients), neuromuscular blockades (1 patient), or infusion of hypertonic saline solution (9 patients). The rest of the cohort underwent ELD after the failure of a second-tier therapy (group 2, 17 cases), mostly barbiturates (15 patients); in 2 patients, an external lumbar drain was placed

after DC for persistent ICH. The median delay significantly differed between the two groups (1 day, range 0–2 days for group 1 vs 2 days, range 1–7 days for group 2; $p = 0.01$). No significant differences (Table 1) were found between groups 1 and 2 in terms of clinical and radiological severity (ISS, PTS, Marshall classification, and Rotterdam score). The mean daily drainage volume was 296 ± 129 ml and the median duration of drainage was 7 ± 5 (range 2–12) days.

Complications

There were 3 cases of cerebellar tonsillar herniation. In these cases, a significant lowering of the cerebellar tonsils according to the McRae line was found between the admission CT scan of the head and control imaging (mean -5 ± 4 vs 9 ± 1 mm, $p = 0.03$). These 3 patients belonged to group 2 ($p = 0.06$) and had diffuse brain swelling with cerebral ischemia. Two of the patients died because of ICH and cerebral ischemia, which were not related to ELD. The patient who survived had a GOS-E score of 5 at follow-up. When analyzing the score proposed by Bauer et al. about the safety of ELD, there was a significant difference between patients with and without tonsillar herniation during ELD (median 3 vs 6, $p = 0.014$).

In the rest of the cohort, there were no significant modification of the level of the tonsils before and after ELD (mean -2.1 ± 2.5 vs -2.4 ± 2.8 mm, mean interval between examinations 11 ± 3 days). No significant difference in mean drained volume was found among patients who showed cerebellar herniation and patients who did not (953 ± 1206 vs 2063 ± 1052 ml, $p = 0.17$; Fig. 1). One lumbar drain had to be changed after 24 hours because of proximal obstruction.

Effect of ELD on ICP and CPP

When analyzing the evolution of ICP and CPP, a significant decrease of mean ICP was found before and after ELD (20.6 ± 5.0 vs 7.2 ± 5.1 mm Hg, $p < 0.001$) with a mean difference of 13.4 ± 6.2 mm Hg. Similarly, there was a significant increase of mean CPP (56.3 ± 6.7 vs 67.0 ± 8.8 mm Hg, $p < 0.001$, mean difference 10.6 ± 6.4 mm Hg; Fig. 2 left). The simple linear logistic regression models showed a significant decrease of ICP and increase of CPP over time ($p < 0.001$; Fig. 2 right).

Outcome and Subgroup Analysis

The overall survival rate was 93% (28/30). Death occurred in 2 cases with refractory ICH following brain edema (Marshall diffuse injury III) treated through burst suppression therapy. An external lumbar drain was placed after the failure of a maximal dose barbiturate coma (mean delay 3.5 days).

Sixteen (53%) of 30 patients did not further need a second-tier treatment for the management of ICH. In group 1, when ELD was performed as part of first-tier treatment, no patient needed escalation of treatment tier ($p < 0.001$). In contrast, only 3 (21%) of the 14 patients in group 2 under barbiturate coma could be weaned off thiopental after external lumbar drain placement, while 1 patient needed DC to control ICH. Both patients who underwent ELD

for refractory ICH after DC needed prolonged burst-suppression therapy. The management strategy is reported in Fig. 3.

The mean duration of intubation was 11.7 ± 7.1 days (2–31). Group 1 patients were extubated earlier (mean 9.0 ± 6.3 vs 14.4 ± 7.2 days, $p = 0.05$). The median GOS-E score at follow-up was 7 (range 1–8) with no difference between the groups (median 7 [range 5–8] vs 7 [range 1–8]). Favorable outcome was achieved in 82% of the cohort.

Discussion

This retrospective series analyzes the outcome of a cohort of 30 pediatric patients with severe TBI who underwent ELD to control refractory ICH. ELD decreased ICP, increased CPP, and notably reduced the level of care when ELD was performed as first-tier therapy. While this study admits limitations due to its retrospective nature, the cohort is homogeneous with a long follow-up period and detailed description of ICP and CPP monitoring, which is currently lacking in the very scarce pediatric literature limited to 2 pediatric^{6,7} and 1 mixed series.¹⁷ Further data dedicated to pediatric TBI are indeed needed, because ICH is challenging in children: slit ventricles render EVD placement hazardous, and posttraumatic hyperemia and brain swelling are more frequent in children than adults (because of stronger carbon dioxide reactivity, more fragile cerebral autoregulation, and physiologically higher cerebral blood flow¹⁸).

Safety of ELD

We confirmed the low complication rate of ELD reported in adult TBI. There was no infection in this series (vs 3.9% in the pooled analysis of Stevens et al.⁵) and 1 patient required early drain revision for proximal obstruction (vs 8% reported). For most patients, there was no significant change in the level of the cerebellar tonsils before and after drain insertion. Cerebellar herniation accounted for 10% of our cohort. As discussed by Stevens et al., the pooled rate of cerebellar herniation after ELD insertion has been reported as 6% (14 of 230 cases, of which 12 came from the German prospective series of 100 patients by Tuettenberg et al.¹⁷). Except for 1 case of iatrogenic disconnection and another of transient fixed dilated pupils 4 hours after drain placement, for the other 12 reported cases the relationship with ELD was doubtful. In our series, cerebellar herniation occurred in the context of massive brain swelling and ischemia (Fig. 1); 2 were lethal and the other had a poor neurological outcome (GOS-E score of 5). In these cases of malignant diffuse edema, cerebellar herniation can occur even without lumbar drainage;^{19,20} this emphasizes the importance of gentle drainage, notably in severe cases. In this regard, our results retrospectively confirm the utility of the score proposed by Bauer et al. assessing the safety of ELD, i.e., in the 3 cases of cerebellar herniation, the Bauer score was ≤ 5 .

Efficacy of ELD

We confirmed that ELD is efficient in improving ICP and CPP, with a mean reduction of ICP of 13.4 mm Hg and increase of CPP of 10.6 mm Hg in this study. Moreover,

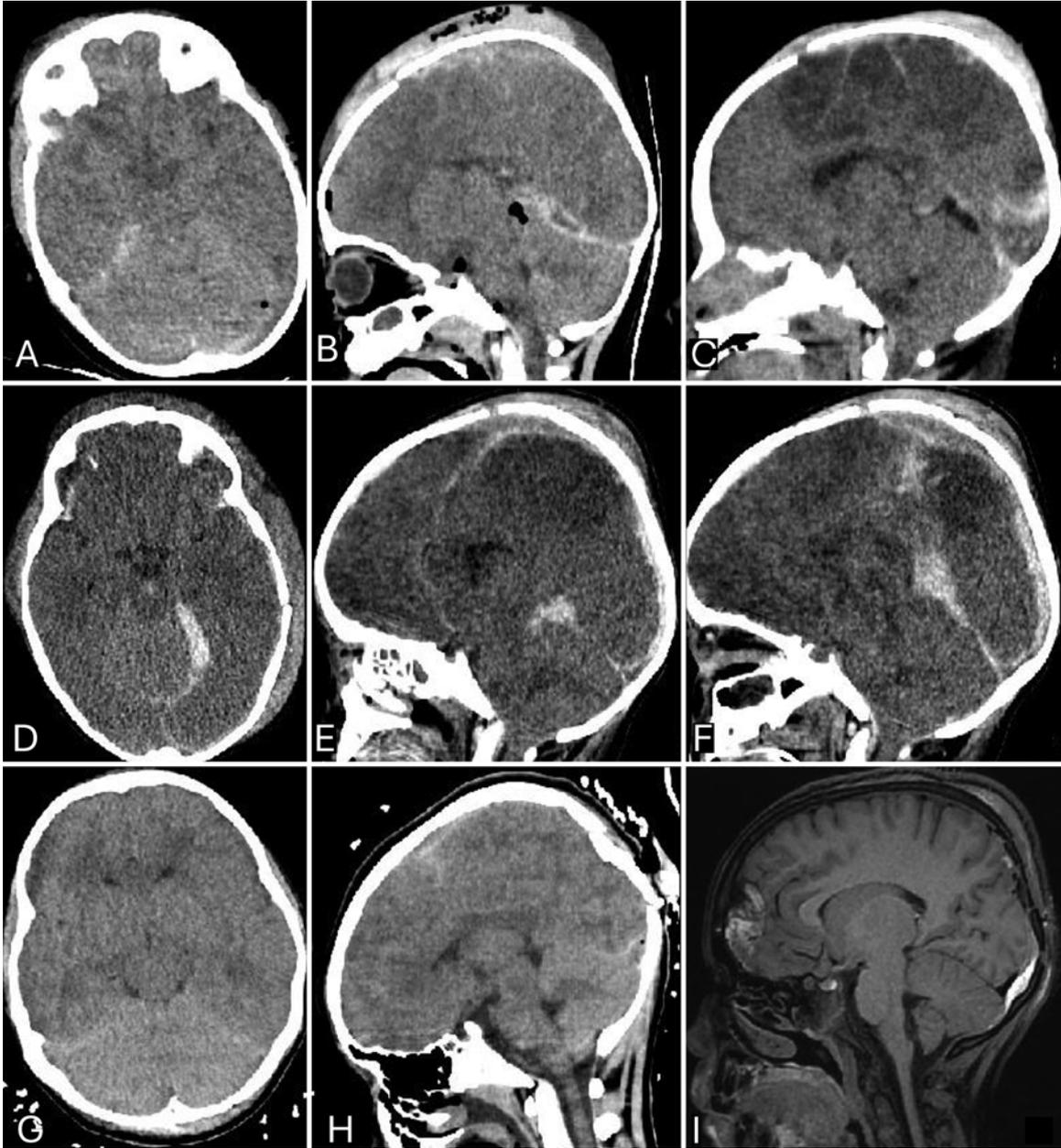


FIG. 1. Images illustrating the radiological evolution of 3 patients undergoing ELD for severe TBI. **A–C:** Images from a 15-month-old victim of a crushing brain injury (from a 30 kg cardboard box that fell from a closet). Axial (A) and sagittal (B) head CT images at admission showed massive diffuse brain swelling, no space-occupying lesion, slit ventricles, and severely compressed cisterns. After 2 days of refractory ICH despite second-tier therapy, an external lumbar drain was placed with a transient effect on ICP and CPP. Five days after admission there was a recurrence of ICH and hemodynamic instability; the sagittal head CT image showed worsening of supratentorial and infratentorial brain swelling, ischemia, and tonsillar herniation (C). The patient died a few days later. **D–F:** Images obtained in a 14-month-old child with severe TBI following defenestration. Initial axial (D) and sagittal (E) head CT images showed diffuse brain swelling with compressed cisterns, parietal ischemia, and cerebellar herniation. Maximal medical treatment failed to control the ICP, so an external lumbar drain was placed 3 days later, with sustained ICP control after 8 days of drainage. The sagittal head CT image (F) 11 days after admission showed persistence of cerebellar herniation. The patient was able to be extubated after 18 days, and at last follow-up (8 years later) showed moderate neurological impairment (GOS-E score = 5). **G–I:** Images in a 2-year-old girl who was a victim of an MVC. Axial (G) and sagittal (H) head CT images at admission documented moderate brain swelling, visible cisterns, and slit ventricles. The patient developed ICH refractory to first-tier therapy. An external lumbar drain was placed 1 day afterwards with successful control of ICP, allowing lowering of sedation and early extubation after 5 days (4 days of drainage). The sagittal brain MR image (I) 5 days after admission showed regression of brain swelling and no changes in the level of the cerebellar tonsils.

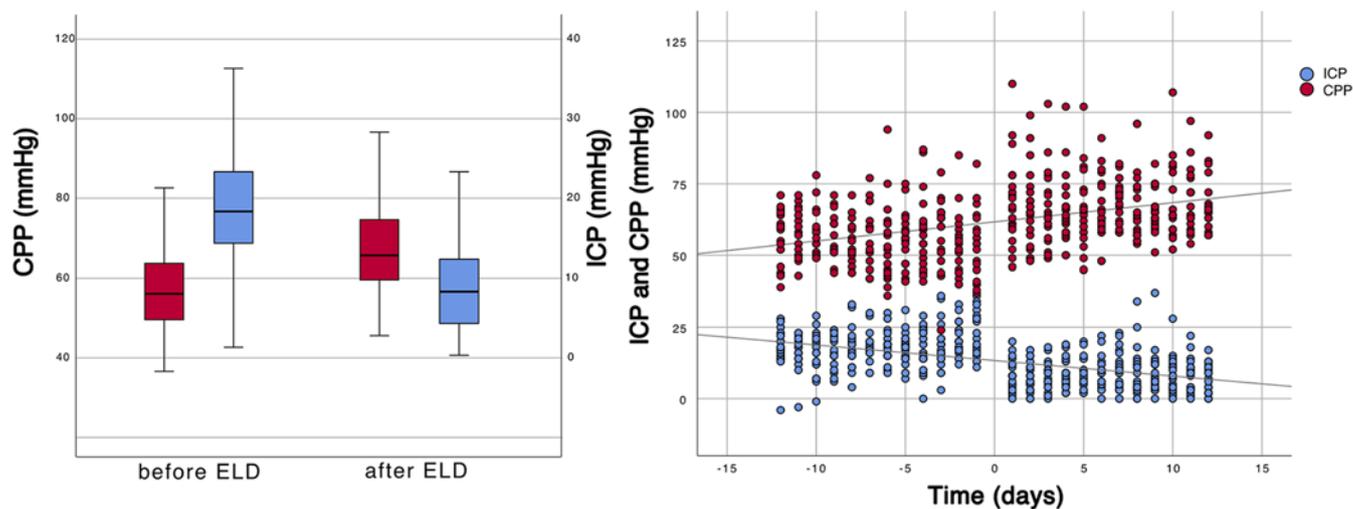


FIG. 2. Graphs showing the effects of ELD placement on ICP and CPP. **Left:** Box-and-whisker plot of the distribution of ICP (blue) and CPP (red) before and after placement of an external lumbar drain. Each box represents the IQR, with the median values indicated by a central line. Whiskers extend from the boxes, showing the minimum and maximum values within 1.5 times the IQR. ICP decreased after ELD (18 ± 9 mm Hg [median \pm IQR] vs 8 ± 8 mm Hg), while CPP increased (5 ± 14 mm Hg vs 65 ± 15 mm Hg). Statistical differences were assessed using a t-student test for paired samples ($p < 0.001$). **Right:** Scatterplot showing the relationship between ICP (blue) and CPP (red) and time with a linear fit line. Each dot represents an individual data point; $R^2 = 0.227$ and 0.152 , respectively. The linear regression model showed that the decrease in ICP and increase in CPP were both significant ($p < 0.001$). Figure is available in color online only.

we showed that 53% of the cohort did not need any further escalation of treatment to control ICH after lumbar drain placement.

All the published studies conclude that there is a beneficial effect of ELD on ICP (and CPP^{7,17,21,22}), but only 4 series analyzed the impact of ELD on the treatment strategy.^{17,21–23} Abadal-Centellas et al. used ELD as a rescue treatment of refractory ICH after a barbiturate coma (median 9 days, range 1–16 days).²² They found that an external lumbar drain helped to reduce mannitol and hypertonic saline infusion and to achieve better control of the barbiturates. In the series of Manet et al., ELD was performed after second-tier therapy (median 5 days, range 4–8 days).²³ They documented a reduction in sedation levels in 75% of the patients within 24 hours. Murad et al. prospectively analyzed the outcome of 15 patients with TBI and subarachnoid hemorrhage (SAH) in which ELD was placed as a first-tier therapy (median 3.8 days, range 1–6 days).²¹ They found a significant reduction in the need for boluses of hypertonic saline/mannitol, sedation, and neuromuscular blockage after lumbar drainage. Finally, in the large prospective series of Tuettenberg et al. (100 patients with TBI and SAH), ELD was performed after the failure of second-tier therapy (median 4 days).¹⁷ Tuettenberg et al. found a correlation between the early withdrawal of therapy after ELD and favorable neurological outcome.

Timing of ELD

We reported a difference in short-term outcome related to the timing of ELD, as all patients who underwent ELD during first-tier therapy achieved sustained control of ICP without needing treatment escalation compared with group 2 patients (only 21% of early weaning from a barbi-

turate coma). Moreover, the mean duration of orotracheal intubation was significantly shorter in these patients (9.0 ± 6.3 vs 14.4 ± 7.2 days, $p = 0.05$). Finally, the 3 patients who developed tonsillar herniation belonged to group 2 ($p = 0.06$). Interestingly, we found no significant difference in clinical and radiological severity scores between the 2 groups. These results suggest a potential benefit in terms of effectiveness and safety of ELD during the first steps of ICH management, as an alternative to EVD in the treatment flowchart. In the literature, only 2 studies enrolled patients in which an external lumbar drain was placed before a barbiturate coma, including 5 of 14 children in the series of Levy et al.⁷ and the 15 patients reported by the prospective cohort of Bauer et al.¹⁶ No comparative analysis was available in the first study, while the second study documented satisfactory ICP control and early reduction of the level of care with no complications reported, except for 1 case of radiological evidence of uncal herniation.

Conclusions

Our study provides preliminary evidence of the efficacy of ELD in decreasing ICP, improving CPP, reducing the need of second-tier treatment, and improving patient outcome. Our results should encourage the use of ELD as part of first-line therapy of posttraumatic ICH, and ELD should be considered a valid alternative to EVD in children without cerebellar herniation and with patent cisterns. Due to the potential risk of herniation, gentle drainage with an ELD level above 5 cm H₂O is mandatory, notably in cases of diffuse brain swelling and ischemia. Larger, multicenter, prospective comparative trials will be needed to validate its use in clinical practice.

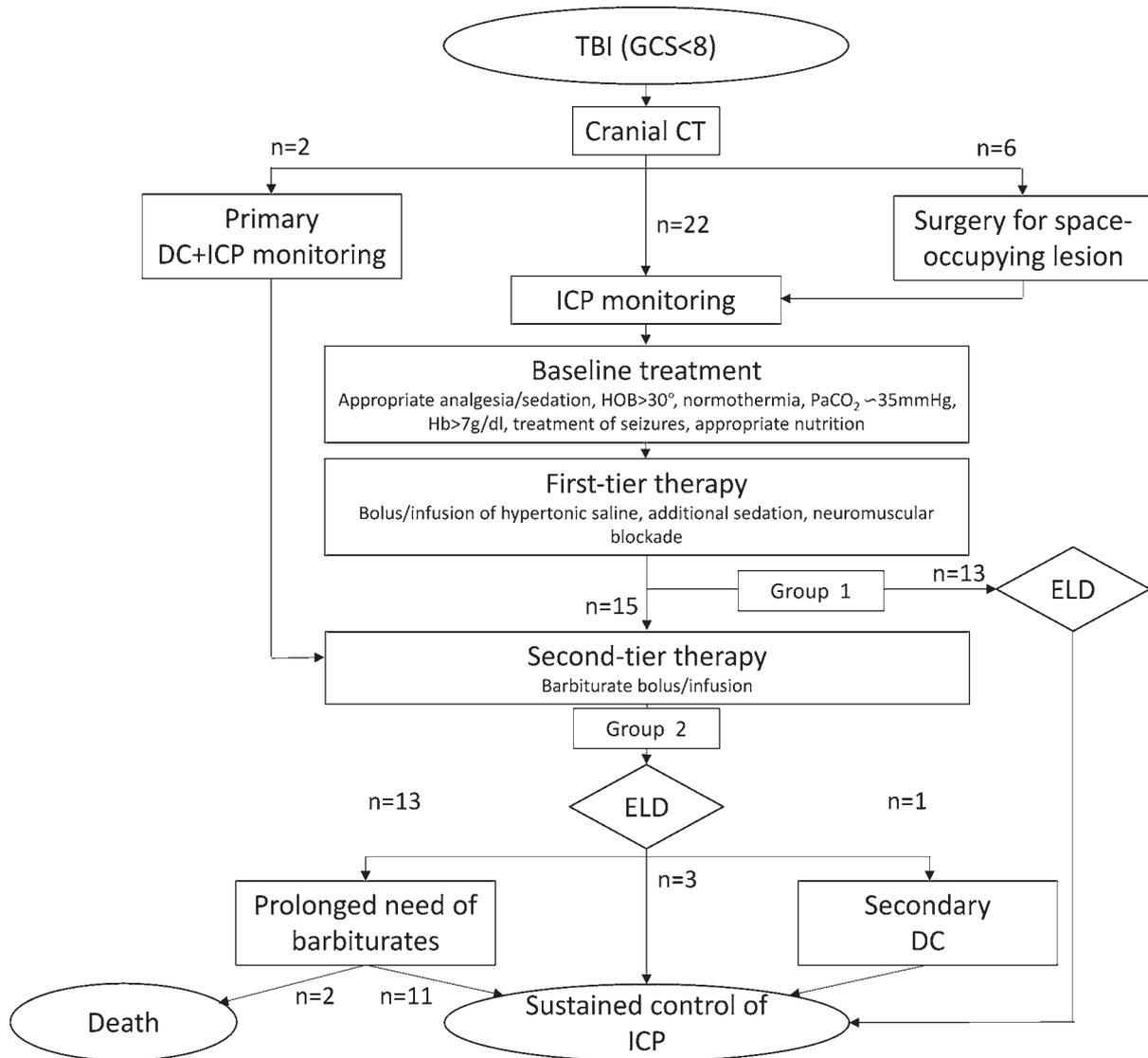


FIG. 3. Chart showing the management strategy and outcome of patients with severe TBI undergoing ELD. ELD was realized as a part of the first-tier therapy of ICH in 13 patients and it allowed a sustained control of the ICP in all patients. Seventeen patients received ELD after the failure of the second-tier therapy; most required prolonged burst-suppression therapy to achieve normal ICP. Hb = hemoglobin; HOB = head of bed.

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Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: Blauwblomme, Guida, Visentin, James, Bourgeois, Beccaria. Acquisition of data: Guida, Visentin, Benichi, Bourgeois, Sauvé-Martin, Dangouloff-Ros. Analysis and interpretation of data: Guida, Benichi, Sauvé-Martin, Vergnaud, Beccaria, Orliaguet. Drafting the article: Blauwblomme, Guida, Benichi, Bourgeois, Sauvé-Martin, Beccaria. Critically revising the article: Blauwblomme, Visentin, Benichi, Paternoster, Sauvé-Martin, Meyer, Vergnaud, Dangouloff-Ros, Beccaria, Orliaguet. Reviewed submitted version of manuscript: Blauwblomme, Benichi, Montmayeur, Dangouloff-Ros, Beccaria, Orliaguet. Statistical analysis: Guida, Benichi. Administrative/technical/material support: Benichi. Study supervision: Blauwblomme.

Supplemental Information

Previous Presentations

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