Child's Nervous System (2019) 35:613–619
https://doi.org/10.1007/s00381-019-04077-4

ORIGINAL ARTICLE

TROPHY registry study design: a prospective, international multicenter study for the surgical treatment of posthemorrhagic hydrocephalus in neonates

Ulrich-Wilhelm Thomale[1] · Giuseppe Cinalli[2] · Abhaya V. Kulkarni[3] · Sara Al-Hakim[1] · Jonathan Roth[4] · Andreas Schaumann[1] · Christoph Bührer[5] · Sergio Cavalheiro[6] · Spyros Sgouros[7] · Shlomi Constantini[4] · Hans Christoph Bock[8]

Received: 16 January 2019 / Accepted: 27 January 2019 / Published online: 6 February 2019

Abstract

Introduction Among children with hydrocephalus, neonates with intraventricular hemorrhage (IVH) and posthemorrhagic hydrocephalus (PH) are considered a group with one of the highest complication rates of treatment. Despite continued progress in neonatal care, a standardized and reliable guideline for surgical management is missing for this challenging condition. Thus, further research is warranted to compare common methods of surgical treatment. The introduction of neuroendoscopic lavage has precipitated the establishment of an international registry aimed at elaborating key elements of a standardized surgical treatment.

Methods The registry is designed as a multicenter, international, prospective data collection for neonates aged 41 weeks gestation, with an indication for surgical treatment for IVH with ventricular dilatation and progressive hydrocephalus. The following initial temporizing surgical interventions, each used as standard treatment at participating centers, will be compared: external ventricular drainage (EVD), ventricular access device (VAD), ventricular subgaleal shunt (VSGS), and neuroendoscopic lavage (NEL). Type of surgery, perioperative data including complications and mortality, subsequent shunt surgeries, ventricular size, and neurological outcome will be recorded at 6, 12, 36, and 60 months.

Results An online, password-protected website will be used to collect the prospective data in a synchronized manner. As a prospective registry, data collection will be ongoing, with no prespecified endpoint. A prespecified analysis will take place after a total of 100 patients in the NEL group have been entered. Analyses will be performed for safety (6 months), shunt dependency (12, 24 months), and neurological outcome (60 months).

Conclusion The design and online platform of the TROPHY registry will enable the collection of prospective data on different surgical procedures for investigation of safety, efficacy, and neurodevelopmental outcome of neonates with IVH and hydrocephalus. The long-term goal is to provide valid data on NEL that is prospective, international, and multicenter. With the comparison of different surgical treatment modalities, we hope to develop better therapy guidelines for this complex neurosurgical condition.

Keywords Cerebrospinal fluid drainage · Neuroendoscopy · Shunt · Reservoir

✉ Ulrich-Wilhelm Thomale
uthomale@charite.de

[1] Pediatric Neurosurgery, Campus Virchow Klinikum, Charité Universitätsmedizin Berlin, Augustenburger Platz 1, 13353 Berlin, Germany

[2] Pediatric Neurosurgery, Santobono-Pausilipon Children's Hospital, Naples, Italy

[3] Division of Neurosurgery, Hospital for Sick Children, University of Toronto, Toronto, ON, Canada

[4] Pediatric Neurosurgery, Dana Children's Hospital, Sourasky Medical Center, Tel Aviv University, Tel Aviv, Israel

[5] Department of Neonatology, Charité Universitätsmedizin Berlin, Berlin, Germany

[6] Neurosurgery, Federal University of Sao Paulo, Sao Paulo, Brazil

[7] Pediatric Neurosurgery, Mitera Children's Hospital, School of Medicine, Athens, Greece

[8] Pediatric Neurosurgery, Universitätsmedizin Göttingen, Göttingen, Germany

Introduction

The treatment of posthemorrhagic hydrocephalus (PH) in premature neonates remains a challenge in many aspects. Both the intraventricular hemorrhage (IVH) and a subsequently developing hydrocephalus are likely to harm the normal neurological development of the child. The early treatment of PH is complicated due to the low body weight of the infant and the bloody ventricular cerebrospinal fluid (CSF) with high protein concentration. Despite ongoing global progress in medicine, a significant rate of neonates continues to suffer from mortality and disability after IVH. Aside from the primary brain damage caused by the hemorrhage itself, secondary brain damage is caused by CSF circulation disturbances, elevation of intracranial pressure (ICP), and inflammatory reactions due to resolution of blood degradation products [1–3]. According to a recent 10-year American health care database study, 9.3% of neonates with IVH of all grades will develop hydrocephalus. Of those, 38.3% will receive a ventricular peritoneal shunt, while 81.7% of those who receive an initial temporizing neurosurgical treatment for PH will develop shunt dependency [4]. Possible complications with CSF shunts include a significant reoperation rate during life-long follow-up [5–7], with neonates with PH being in the group with the highest rate of shunt complications [8–13]. The goal remains to enhance the neurodevelopmental outcome by reducing the complications during treatment, to prevent further progression of hydrocephalus, and to reduce the rate of shunt dependency, as well as the rate of surgical revisions linked to the CSF diverting implant [14–16].

With the presented collaborative effort, we defined the need for a comparative prospective synchronized data collection for different types of initial neurosurgical treatment for neonates with posthemorrhagic hydrocephalus. Our aim with the TROPHY study is to collect relevant data on safety, efficacy, and long-term neurodevelopmental outcome of four different initial treatment methods, included in a frame of a multicenter international registry.

Methods

International collaboration

Under the umbrella of the International Federation of Neuroendoscopy (previously the International Study Group for Neuroendoscopy), pediatric neurosurgical centers throughout the world have already conducted a number of collaborative studies, creating an established network of collaborating clinicians. The first study dealt with the merits of repeat-endoscopic third ventriculostomy in 20 patients from 4 centers [17]. The second study dealt with endoscopic third ventriculostomy (ETV) following infection and/or hemorrhage in 101 patients from 7 centers [18]. The third study was conducted on safety and accuracy of neuroendoscopic biopsies and included 293 patients in 13 centers [19]. The fourth study was the International Infant Hydrocephalus Study (IIHS), which included 158 patients from 27 centers and compared ETV and shunt for infant hydrocephalus [20, 21]. Uniquely, the IIHS was prospective, which has set the stage for the current proposed prospective registry. We have thus proved our commitment and ability to collaborate and collect relevant data internationally. Such multicenter studies allow an accelerated rate of data collection for rare diseases or surgical procedures. Not only that, but the data provided are more generalizable and universally applicable.

Rationale and concept of the TROPHY registry

The heterogeneity of approaches to surgically treat posthemorrhagic hydrocephalus in neonates and the lack of data for safety and efficacy of the different treatment options warrant a prospective data acquisition on this topic. Different established surgical approaches like external ventricular drainage (EVD), ventricular access device (VAD), and ventriculosubgaleal shunt (VSGS) have never been compared in a comparative prospective investigation for complication rate and neurological outcome parameters. A meta-analysis investigation from historical cohort studies showed a higher mortality (19.1%) and revision rate (47.3%) for EVDs, however with a diminished shunt rate (68.2%) [22]. A new technique of neuroendoscopic lavage (NEL) appears to be a safe and effective treatment modality to diminish the intraventricular blood and achieve CSF relief as shown in a retrospective single-center study, but requiring further evaluation on a multicenter basis [23]. A more recent bi-center report combined the experience from two centers reporting a mortality rate of 5.4%, a re-bleeding rate with surgical indication of 3.6%, a shunt rate of 57%, and a shunt revision rate of 1.7 ± 1.9 during the first 12 months in a cohort of 56 neonates [24].

Recommendations from the hydrocephalus guidelines are rather limited [15]. This clearly highlights the necessity for a multicenter, prospective registry in order to provide standardized data collection on different treatment modalities for posthemorrhagic hydrocephalus in neonates.

We decided after intense discussion against a randomized study approach due to the following reasons: (1) The IIHS study showed very limited compliance of parents and caretakers to agree on randomization, with parental preference strongly dictating treatment. (2) Some centers with standard protocols are unable to switch their treatment regimen away from a standard procedure, so institutional compliance would also be limited. Thus, it was decided to perform a comprehensive online registry for multicenter prospective data collection in order to analyze immediate and long-term outcome of neonates with IVH and progressive hydrocephalus and to

compare NEL with other established treatment options among the participating centers. Outcome parameters include surgical complications, mortality, shunt dependency, ventricular size, and neurological outcome. A synchronized collection of patient data from participating centers will establish an international comparative database.

Results

The TROPHY registry is a password-protected online database, with individual access for the respective individuals of the participating centers. Possible initial neurosurgical techniques are EVD, VAD, VSGS, and NEL, which will be subsequently compared in the analysis of the study data (Fig. 1). The registry is structured to include patient characteristics, preoperative status, imaging, operative techniques, complications, and reoperations, as well as 6, 12, 24, 36, and 60 months follow-up measuring shunt dependency, shunt revision rate, and neurological outcome. The data will be pseudonymized and are entered into the database by investigators of each participating hospital. The centers' investigators with access to the database are enabled to review only their own data. The principle investigators (administrator) located at the Charité Universitätsmedizin, Berlin, and Universitätsmedizin Göttingen, Germany, will manage the entire dataset and oversee the analyses at the predefined time points for later statistical analysis.

Administration

Data recording and collection will be accomplished by a study-database application based on Filemaker® software allowing individualized username- and password-protected access only for registered participants and administrative staff. The central data server is physically located and expertly hosted at the Charité, Berlin, Germany, to provide online access to the study database-application via Filemaker® Server software. Data transfer between the clinical server and the study server is encrypted (SSL coding) to assure data privacy. Access to the online registry application is provided over the study homepage: http://trophy-registry.org (Fig. 2).

All clinical data of affiliated patients are assigned to an automatically generated Case-ID (pseudonym). Clinical data is directly entered online into the study database application by the investigating physicians. Registered study participants can create multiple datasets and complement or update the corresponding clinical data content prospectively at any time by their individual log-in. All documents concerning patients' treatment-related data are linked to the Case-ID and are recorded in folders of the Electronic Case Report Forms (eCRF).

As soon as a follow-up form has to be filled in, the participating department will be informed with an e-mail and a reminder will be sent after 2 weeks. Issues with data entry compliance and integrity could lead to expulsion of a center from the registry by the steering committee. The online Web-based registry for recruitment and data collection will enable

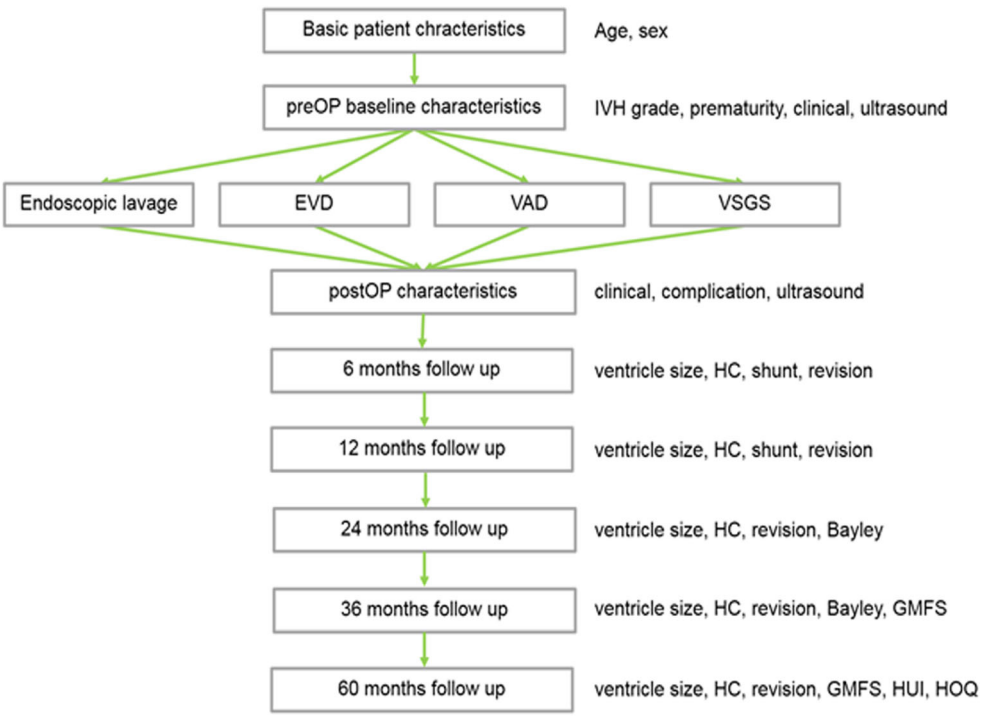

Fig. 1 Flowchart of TROPHY registry design

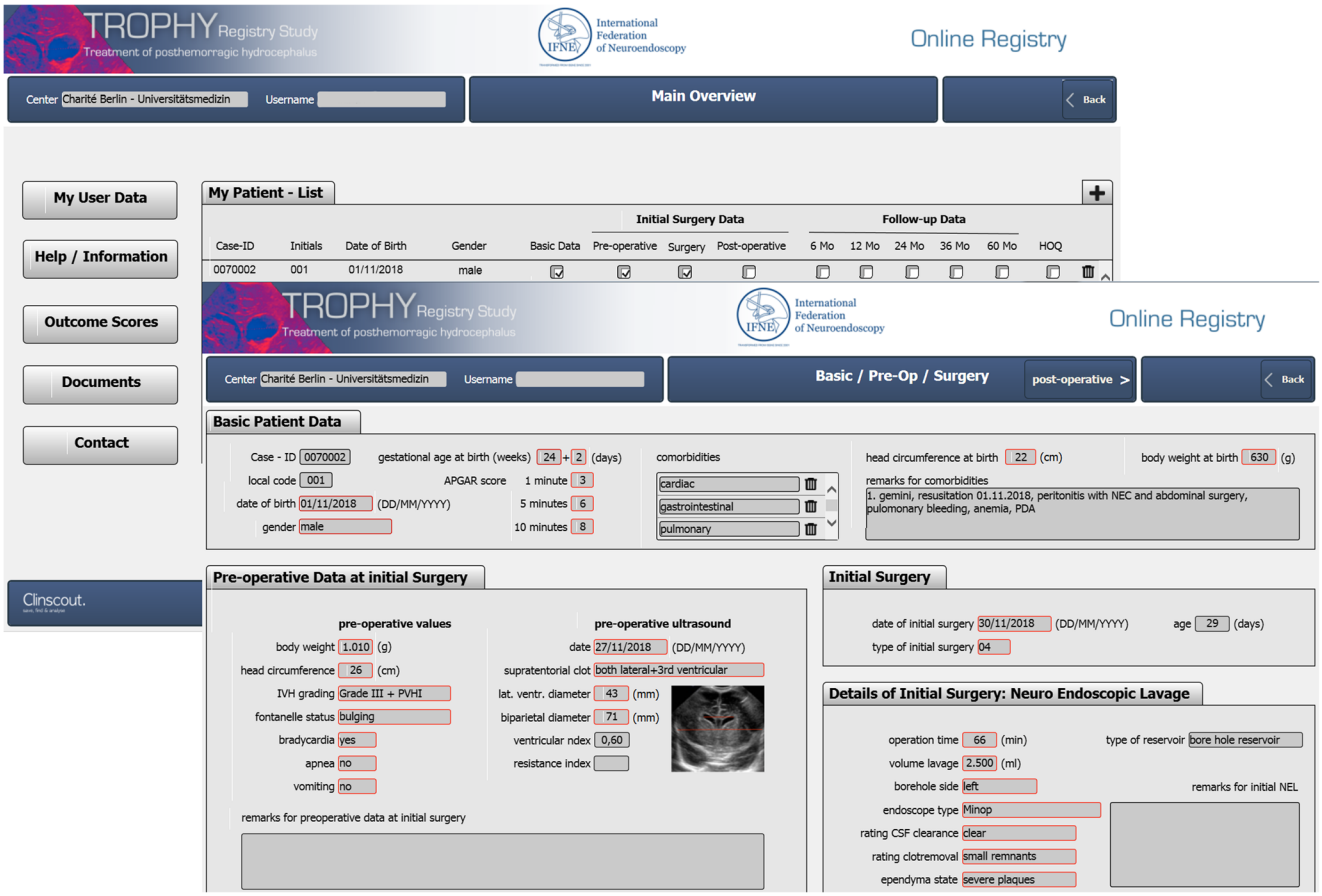

Fig. 2 Representative screenshots of the online registry (https://trophy-registry.org) referring to the patient list overview and the basic data entry for perioperative clinical condition and surgical technique used

contemporaneous data entry and improved completeness, as the user is obliged to complete required fields before proceeding to the subsequent steps. In addition, it will allow the administrators to have a real-time view of recruited patients; their eligibility and appropriate guidance for the participating centers may be provided through the study at any time.

Inclusion and exclusion characteristics

Surgical interventions eligible for patient inclusion in the TROPHY registry are NEL, EVD, VAD, and VSGS, performed according to standard local procedure of the participating center. The participating centers who offer NEL as a surgical intervention have neuroendoscopic and pediatric neurosurgical expertise with more than 10 neurosurgical procedures in neonates per year per surgeon. Completion of a training workshop on NEL is highly recommended before starting this technique and at least one NEL surgery in neonates per surgeon per year is required. A strong commitment to the study design, consent, follow-up, and smooth data supply and the ability to follow-up for at least 5 years are required for every medical center.

Inclusion in the TROPHY registry study will be achieved by written and signed consent by parents or caretakers to this project.

The clinical condition of the patient must meet the following criteria for *inclusion*:

- No previous surgical treatment for hydrocephalus
- Gestational age ≤ 41 weeks at first neurosurgical intervention
- IVH documented by ultrasonography
- Hydrocephalus with progressing ventricular size (US ventricular indices above 97th percentile; according to Levene) diagnosed by preoperative ultrasonography
- Surgically treated with any of the following: NEL, EVD, VAD, VSGS
- Ability to follow-up 5 years after initial surgical treatment

The following criteria for *exclusion* must be absent:

- Comorbidity-related instability forbidding surgical intervention
- Diagnosed impaired hemostasis in the most recent laboratory results within up to 5 days before surgery (platelet

counts < 50,000/ml; prothrombin time (Quick) > 20 s; PTT > 50 s)
- Proven CNS tumor or vascular malformation

Outcome parameters

For each patient registered into the TROPHY registry, we are combining a primary factor together with a weighted set of secondary factors to reach meaningful measures of the treatment quality and patient outcome.

The primary outcome for each study participant is based on the neurobehavioral outcome when the patient reaches 5 years of age.

The secondary outcomes include the following factors: number of hydrocephalus-related operations; surgical morbidity; initial intensive care hospitalization time; need for second surgery at follow-up; radiological measures of hydrocephalus; mortality; complications such as CNS infection, secondary hemorrhage, seizures requiring medications.

Neurodevelopmental aspects

The long-term neurodevelopmental effects of the primary damage of hemorrhage and comorbidities, as well as of any surgical intervention, are a major concern for the group of neonates. Comprehensive, standardized evaluation of the participants' development and abilities over the follow-up course is an essential element of this registry, since the primary criteria for each intervention are based on the neurobehavioral outcome when the patient reaches 5 years of age.

For this reason, a schedule of careful assessments of each child's development is included in this registry. We have chosen a set of comprehensive, objective evaluation tests that are standardized, with consistent numeric scoring scales, to enable objective, statistically meaningful comparisons and analyses of the results, for a large patient body that is drawn from a broad range of places over an extended period of time. Post-operative, ongoing evaluations are planned to track the patient's development and progress over time on a regular basis. Testing is scheduled at regular intervals after 24, 36, and 60 months of follow-up.

Developmental assessments are based on the following:

- At the time of 24 and 36 months of follow-up, the Bayley Scale of Infant Development (BSID) and the Gross Motor Function Classification System (GMFCS) will be used. Due to the extended efforts required of the BSID, which might not be available at all centers, this item will be strongly recommended, but is not defined as mandatory.
- After 60 months of follow-up, the Gross Motor Function Classification System (GMFCS) will be used, in addition to the Health Utility Index (HUI®) and the Hydrocephalus Outcome Questionnaire (HOQ) for evaluation of the neurological outcome and quality of life.

Statistical considerations

As a prospective registry, data collection will be ongoing, with no prespecified endpoint for data collection. Because it is unclear how many patients with VAD, VSGS, and EVD will be recruited, we are not prespecifying a strictly defined comparative analysis. According to the present information, the following analyses shall be made:

Analysis of complication incidence Assuming the incidence of each possible complication will not be greater than 0.1 and aiming for an estimate precision of ± 0.05 (95% confidence interval), this analysis will be conducted after 139 patients following NEL have reached 6 months follow-up. An estimate for each of the following complications will be calculated and compared to the other surgical techniques: infection, reoperation, subcutaneous CSF collection, CSF fistula, re-hemorrhage, mortality.

Analysis of shunt dependency An estimate of the incidence of patients requiring shunt after NEL will be conducted and compared to the other surgical techniques. Assuming a shunt dependency incidence of approximately 0.6 and aiming for an estimate precision of ± 0.1 (95% confidence interval), this analysis will be conducted after 100 patients following NEL have reached 12 months follow-up.

Analysis of long-term developmental outcome Developmental outcome will be analyzed as follows: Bayley Scale of Infant Development, 3rd Edition, Scale Scorers, at 24 months and 36 months; GMFCS at 24, 36, and 60 months; Health Utilities Index-Mark 3 at 60 months; Hydrocephalus Outcome Questionnaire at 60 months. The aforementioned outcome parameters will be analyzed once at least 100 patients have been assessed for the respective outcome.

Discussion

Neurosurgical treatment of posthemorrhagic hydrocephalus in neonates remains challenging in the context of high comorbidities of these patients with very low body weight and high CSF protein polluted CSF. Thus, initial temporizing neurosurgical treatment is mostly applied before patients are eligible for possible shunting procedures. These procedures include EVD, VAD, and VSGS and are associated with relevant perioperative complications [22]. Until today, no relevant guidelines or any consensus is given in the literature for this rather complex clinical condition [11, 25–28]. A meta-analysis was able to make the following very limited recommendations. First, clinical judgment is necessary for the decision regarding which temporizing measure is applied among the possibilities of EVD, VAD, VSGS, or even lumbar puncture (LP). The latter one, however, is not considered as a neurosurgical

intervention and is not recommended as a serial treatment option especially if non-communicating hydrocephalus is present. Second, VSGS reduces the amount of daily CSF aspirations compared to VAD, whereas VAD reduces the morbidity and mortality compared to EVD. However, all recommendations are linked with only a moderate degree of clinical certainty. Therefore, the need for better evidence in these complex cases remains essential [15].

Recently, some promising results were reported by applying neuroendoscopic lavage in neonates with posthemorrhagic hydrocephalus as the initial neurosurgical treatment option [23]. The data available for this technique is certainly limited since it was collected in only a few centers, but the potential advantages include a possibly reduced rate of shunt dependency, infection, and mortality, as well as a possible reduction in subsequent complications for shunted patients. However, in order to draw a clear conclusion on this technique, a multicenter approach and further clinical evaluation is warranted.

By introducing the multicenter prospective TROPHY registry, we aim to achieve statistically meaningful results for issues that to date have had no objective basis for solid interpretation. The registry is the only comprehensive database to date that focuses on long-term developmental outcomes for neonates with posthemorrhagic hydrocephalus in relation to the applied intervention. As such, the TROPHY registry will serve as an essential tool, providing any means for better parental counseling and for defining standards on the treatment of this challenging patient group. As was already established in previous studies, the registry will further strengthen international collaboration in the field of a rare condition and can settle important debates in a scientific manner. The international framework that we construct with the TROPHY registry will as well serve as a platform for future prospective studies.

Compliance with ethical standards

Conflict of interest This registry received an initial financial support by B. Braun foundation. B. Braun does not hold any rights on the registry. No other conflict of interest according to the content of this paper is declared.

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

References

1. Jin DL, Christian EA, Attenello F, Melamed E, Cen S, Krieger MD, McComb JG, Mack WJ (2016) Cross-sectional analysis on racial and economic disparities affecting mortality in preterm infants with posthemorrhagic hydrocephalus. World Neurosurg 88:399–410
2. Burstein J, Papile LA, Burstein R (1979) Intraventricular hemorrhage and hydrocephalus in premature newborns: a prospective study with CT. AJR Am J Roentgenol 132(4):631–635
3. Limbrick DD Jr, Mathur A, Johnston JM, Munro R, Sagar J, Inder T et al (2010) Neurosurgical treatment of progressive posthemorrhagic ventricular dilation in preterm infants: a 10-year single-institution study. J Neurosurg Pediatr 6(3):224–230
4. Christian EA, Melamed EF, Peck E, Krieger MD, McComb JG (2016) Surgical management of hydrocephalus secondary to intraventricular hemorrhage in the preterm infant. J Neurosurg Pediatr 17(3):278–284
5. Spader HS, Hertzler DA, Kestle JR, Riva-Cambrin J (2015) Risk factors for infection and the effect of an institutional shunt protocol on the incidence of ventricular access device infections in preterm infants. J Neurosurg Pediatr 15(2):156–160
6. Albright AL, Haines SJ, Taylor FH (1988) Function of parietal and frontal shunts in childhood hydrocephalus. J Neurosurg 69(6):883–886
7. Sasidharan P, Marquez E, Dizon E, Sridhar CV (1986) Developmental outcome of infants with severe intracranial-intraventricular hemorrhage and hydrocephalus with and without ventriculoperitoneal shunt. Child's nervous system: ChNS: official journal of the International Society for Pediatr Neurosurg 2(3):149–152
8. Adams-Chapman I, Hansen NI, Stoll BJ, Higgins R (2008) Neurodevelopmental outcome of extremely low birth weight infants with posthemorrhagic hydrocephalus requiring shunt insertion. Pediatrics 121(5):e1167–e1177
9. Gebert AF, Schulz M, Haberl H, Thomale UW (2013) Adjustments in gravitational valves for the treatment of childhood hydrocephalus-a retrospective survey. Child's nervous system: ChNS: official journal of the International Society for Pediatr Neurosurg 29(11):2019–2025
10. Alan N, Manjila S, Minich N, Bass N, Cohen AR, Walsh M, Robinson S (2012) Reduced ventricular shunt rate in very preterm infants with severe intraventricular hemorrhage: an institutional experience. J Neurosurg Pediatr 10(5):357–364
11. Horinek D, Cihar M, Tichy M (2003) Current methods in the treatment of posthemorrhagic hydrocephalus in infants. Bratisl Lek Listy 104(11):347–351
12. Boynton BR, Boynton CA, Merritt TA, Vaucher YE, James HE, Bejar RF (1986) Ventriculoperitoneal shunts in low birth weight infants with intracranial hemorrhage: neurodevelopmental outcome. Neurosurgery 18(2):141–145
13. Miranda P (2010) Intraventricular hemorrhage and posthemorrhagic hydrocephalus in the preterm infant. Minerva Pediatr 62(1):79–89
14. Wellons JC, Shannon CN, Kulkarni AV, Simon TD, Riva-Cambrin J, Whitehead WE, Oakes WJ, Drake JM, Luerssen TG, Walker ML, Kestle JR, Hydrocephalus Clinical Research Network (2009) A multicenter retrospective comparison of conversion from temporary to permanent cerebrospinal fluid diversion in very low birth weight infants with posthemorrhagic hydrocephalus. J Neurosurg Pediatr 4(1):50–55
15. Mazzola CA, Choudhri AF, Auguste KI, Limbrick DD Jr, Rogido M, Mitchell L et al (2014) Pediatric hydrocephalus: systematic literature review and evidence-based guidelines. Part 2: management of posthemorrhagic hydrocephalus in premature infants. J Neurosurg Pediatr 14(Suppl 1):8–23
16. Paraicz E (1979) Successful treatment of perinatal intraventricular haemorrhage. Acta Paediatr Acad Sci Hung 20(2–3):211–214
17. Siomin V, Weiner H, Wisoff J, Cinalli G, Pierre-Kahn A, Saint-Rose C et al (2001) Repeat endoscopic third ventriculostomy: is it worth trying? Childs Nerv Syst 17(9):551–555
18. Siomin V, Cinalli G, Grotenhuis A, Golash A, Oi S, Kothbauer K, Weiner H, Roth J, Beni-Adani L, Pierre-Kahn A, Takahashi Y, Mallucci C, Abbott R, Wisoff J, Constantini S (2002) Endoscopic third ventriculostomy in patients with cerebrospinal fluid infection and/or hemorrhage. J Neurosurg 97(3):519–524

19. Constantini S, Mohanty A, Zymberg S, Cavalheiro S, Mallucci C, Hellwig D et al (2013) Safety and diagnostic accuracy of neuroendoscopic biopsies: an international multicenter study. J Neurosurg Pediatr 11(6):704–709
20. Kulkarni AV, Sgouros S, Constantini S (2016) International Infant Hydrocephalus Study: initial results of a prospective, multicenter comparison of endoscopic third ventriculostomy (ETV) and shunt for infant hydrocephalus. Childs Nerv Syst 32(6):1039–1048
21. Kulkarni AV, Sgouros S, Constantini S (2017) Outcome of treatment after failed endoscopic third ventriculostomy (ETV) in infants with aqueductal stenosis: results from the International Infant Hydrocephalus Study (IIHS). Childs Nerv Syst 33(5):747–752
22. Badhiwala JH, Hong CJ, Nassiri F, Hong BY, Riva-Cambrin J, Kulkarni AV (2015) Treatment of posthemorrhagic ventricular dilation in preterm infants: a systematic review and meta-analysis of outcomes and complications. J Neurosurg Pediatr 16(5):545–555
23. Schulz M, Buhrer C, Pohl-Schickinger A, Haberl H, Thomale UW (2014) Neuroendoscopic lavage for the treatment of intraventricular hemorrhage and hydrocephalus in neonates. J Neurosurg Pediatr 13(6):626–635
24. d'Arcangues C, Schulz M, Buhrer C, Thome U, Krause M, Thomale UW (2018) Extended experience with neuroendoscopic lavage for posthemorrhagic hydrocephalus in neonates. World Neurosurg 116:e217–ee24
25. Bock HC, Feldmann J, Ludwig HC (2018) Early surgical management and long-term surgical outcome for intraventricular hemorrhage-related posthemorrhagic hydrocephalus in shunt-treated premature infants. J Neurosurg Pediatr 22(1):61–67
26. de Vries LS, Liem KD, van Dijk K, Smit BJ, Sie L, Rademaker KJ et al (2002) Early versus late treatment of posthaemorrhagic ventricular dilatation: results of a retrospective study from five neonatal intensive care units in The Netherlands. Acta Paediatr 91(2):212–217
27. Gurtner P, Bass T, Gudeman SK, Penix JO, Philput CB, Schinco FP (1992) Surgical management of posthemorrhagic hydrocephalus in 22 low-birth-weight infants. Childs Nerv Syst 8(4):198–202
28. Kormanik K, Praca J, Garton HJ, Sarkar S (2010) Repeated tapping of ventricular reservoir in preterm infants with post-hemorrhagic ventricular dilatation does not increase the risk of reservoir infection. J Perinatol 30(3):218–221