Child's Nervous System (2019) 35:1283–1293
https://doi.org/10.1007/s00381-019-04203-2

REVIEW ARTICLE

Endoscopic third ventriculostomy versus shunt for pediatric hydrocephalus: a systematic literature review and meta-analysis

Pavlos Texakalidis[1] · Muhibullah S. Tora[1] · Jeremy S. Wetzel[1] · Joshua J. Chern[1,2]

Received: 19 March 2019 / Accepted: 9 May 2019 / Published online: 25 May 2019

Abstract

Background Optimized management of pediatric hydrocephalus remains the subject of debate. Ventriculoperitoneal shunt is largely considered the standard of care. However, the advancements and introduction of new cerebrospinal fluid (CSF) diversion approaches including the use of endoscopic third ventriculostomy (ETV) offer appealing alternatives that have been reported in numerous observational series.

Objective To evaluate the comparative safety and efficacy of shunting and ETV in pediatric hydrocephalus cases.

Methods This systematic literature review was performed according to the PRISMA guidelines. Eligible studies were identified through a search of PubMed (Medline) and Cochrane until October 2018. A random effects model meta-analysis was conducted and the I-square was used to assess heterogeneity. The ROBINS-1 tool and Cochrane tool were used to assess risk of bias in the observational and randomized studies, respectively.

Results Fourteen studies including 8419 patients were identified. Patients in the ETV group had a statistically significant lower risk of infection compared to shunt (OR: 0.19; 95% CI: 0.07–0.53; I^2: 0%). All-cause mortality (OR: 0.77; 95% CI: 0.35–1.68; I^2: 0%), post-operative CSF leak (OR: 1.53; 95% CI: 0.37–6.31; I^2: 0%), and reoperation rates were similar between the two study groups (OR: 0.72; 95% CI: 0.39–1.32; I^2: 93.5%). Subgroup analyses for re-operation demonstrated that ETV in Africa (OR: 0.13; 95% CI: 0.03–0.48; I^2: 0%) and Europe (OR: 0.39; 95% CI: 0.30–0.52; I^2:1.4%) was associated with significantly lower odds of re-operation compared to shunt, but not in USA/Canada (OR: 1.49; 95% CI: 0.85–2.63; I^2:86.2%). Meta-regression analyses of age and duration of follow-up did not affect re-operation rates.

Conclusions ETV was associated with a statistically significant lower risk of procedure-related infection compared to shunt. All-cause mortality, CSF leak, and re-operation rates were similar between the study groups. Subgroup analysis based on the geographic region showed that ETV is associated with statistically significant lower odds for re-operation in Europe and Africa, but not in USA/Canada. Future RCTs are needed to validate the results of this study and elucidate the cause of this heterogeneity.

Keywords Endoscopic third ventriculostomy · Choroid plexus cauterization · Shunt · Shunting · Hydrocephalus

Prior Publication or Presentation
No portion of this paper has been previously presented or published in any academic or clinical proceedings or journals.

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s00381-019-04203-2) contains supplementary material, which is available to authorized users.

✉ Pavlos Texakalidis
ptexaka@emory.edu

1 Department of Neurosurgery, Emory University School of Medicine, Suite 6204, 101 Woodruff Circle, Atlanta, GA 30322, USA

2 Children's Healthcare of Atlanta, Department of Neurosurgery, Egleston Hospital, Atlanta, GA, USA

Introduction

Hydrocephalus in children remains one of the more common etiologies for admission in the pediatric neurosurgical units. [1] Ventriculoperitoneal shunt (VPS) is considered the standard of care, despite the advancements and introduction of new cerebrospinal fluid (CSF) diversion approaches in hydrocephalus' neurosurgical management, including the endoscopic third ventriculostomy (ETV). [2, 3] Nevertheless, VPS is associated with significant complications including shunt malfunction, infections, and inconsistent long-term motor and cognitive outcomes. [4] Several studies have evaluated the current shunt success and failure rates as compared to those of the past decades; however, results are inconclusive in the literature. [5, 6]

ETV has emerged as an alternative CSF diversion procedure especially in non-communicating hydrocephalus cases [7, 8]; however, it has been suggested that ETV might also be beneficial for some pediatric patients with communicating hydrocephalus. [9, 10] Recently, the addition of choroid plexus cauterization (CPC) during ETV has been reported to improve the efficacy of the endoscopic approach. [11, 12] This increasing interest is reflected by the emerging number of studies evaluating the comparative effectiveness of VPS and ETV. [13, 14]

The aims of this study are to systematically review the literature and evaluate the comparative safety and efficacy of shunting and ETV in pediatric hydrocephalus cases. Knowing the limitations of mixed hydrocephalus etiology, geographical location, and changes in the performance of ETV, this study tries to investigate their effect by conducting subgroup analyses.

Methods

This systematic review and meta-analysis was performed according to the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) guidelines. [15]

Search strategy and selection criteria

Systematic searches were conducted in PubMed (Medline) and Cochrane Databases. The keywords used for PubMed were "endoscopic third ventriculostomy", "shunt", "children", "infants", "neonates", and "pediatric". The search was conducted by two independent investigators (PT, MT). Any disagreements or discrepancies were resolved by consensus. The references of the included studies were also manually reviewed in order to identify further eligible articles.

A study was included in this meta-analysis if it fulfilled four predefined criteria: (i) randomized controlled trials (RCT) or prospective and retrospective observational analyses comparing the shunting vs ETV (with or without CPC); (ii) studies that reported quantitative data on clinical outcomes of interest; and (iii) studies published up to October 2018. When duplicates were identified, the most recent analysis was included unless the earliest version reported more relevant outcomes.

Data extraction and outcomes

Two reviewers, blind to each other (PT, MT), independently extracted the relevant data from the eligible studies. Variables abstracted were first author, year of publication, years of enrollment, country, design of study, study arms, hydrocephalus etiology, age, gender, failure rates, CSF leak, infection, mortality, re-operation, shunt malfunction, and intraventricular hemorrhage. All disagreements were resolved following discussion and final decision was reached by consensus. The primary outcome was incidence of infection. A standardized definition for infection could not be provided due to lack of reporting by the included studies. Secondary outcomes were all-cause mortality, CSF leak, and the need for re-operation. Re-operation in both groups was defined as the need for any second operation either shunt or ETV during the follow-up period.

Risk of bias assessment

Risk of bias was assessed by two investigators (PT, MT) with the Robins-I tool for non-randomized studies. [16] The following domains for the non-randomized studies were evaluated: confounding, selection of participants, departure from intended interventions, missing data, measurement of outcomes, and selective reporting. RCTs were assessed with the Cochrane tool. [17] Discrepancies in quality assessment were resolved via consensus.

Statistical synthesis and analysis

Odds ratios (ORs) with the corresponding 95% confidence intervals (CIs) were used for the outcomes. A random effects model was used to account for heterogeneity among studies. Heterogeneity was assessed with the Higgins I-square statistic. [18] I^2 greater than 50% indicated significant heterogeneity. [18] Forest plots were used to graphically display the effect size in each study and the pooled estimates. Meta-regression analysis was performed to adjust for the age and various follow-up intervals as a study level covariates. A p value of < 0.05 was considered significant. STATA 14.1 (StataCorp, College Station, Texas) statistical software was used for all analyses.

Results

Search results

Literature search yielded 683 potentially relevant records after duplicates were removed. After screening titles and abstracts, 18 articles were retrieved for full-text evaluation. Fourteen studies met the predetermined eligibility criteria and were included in the meta-analysis as shown in the PRISMA flow diagram (Fig. 1).

Characteristics of the included studies

This meta-analysis of 14 studies comprised 8419 patients overall (ETV: 1994; shunt: 6425 patients). [1, 3, 13, 14,

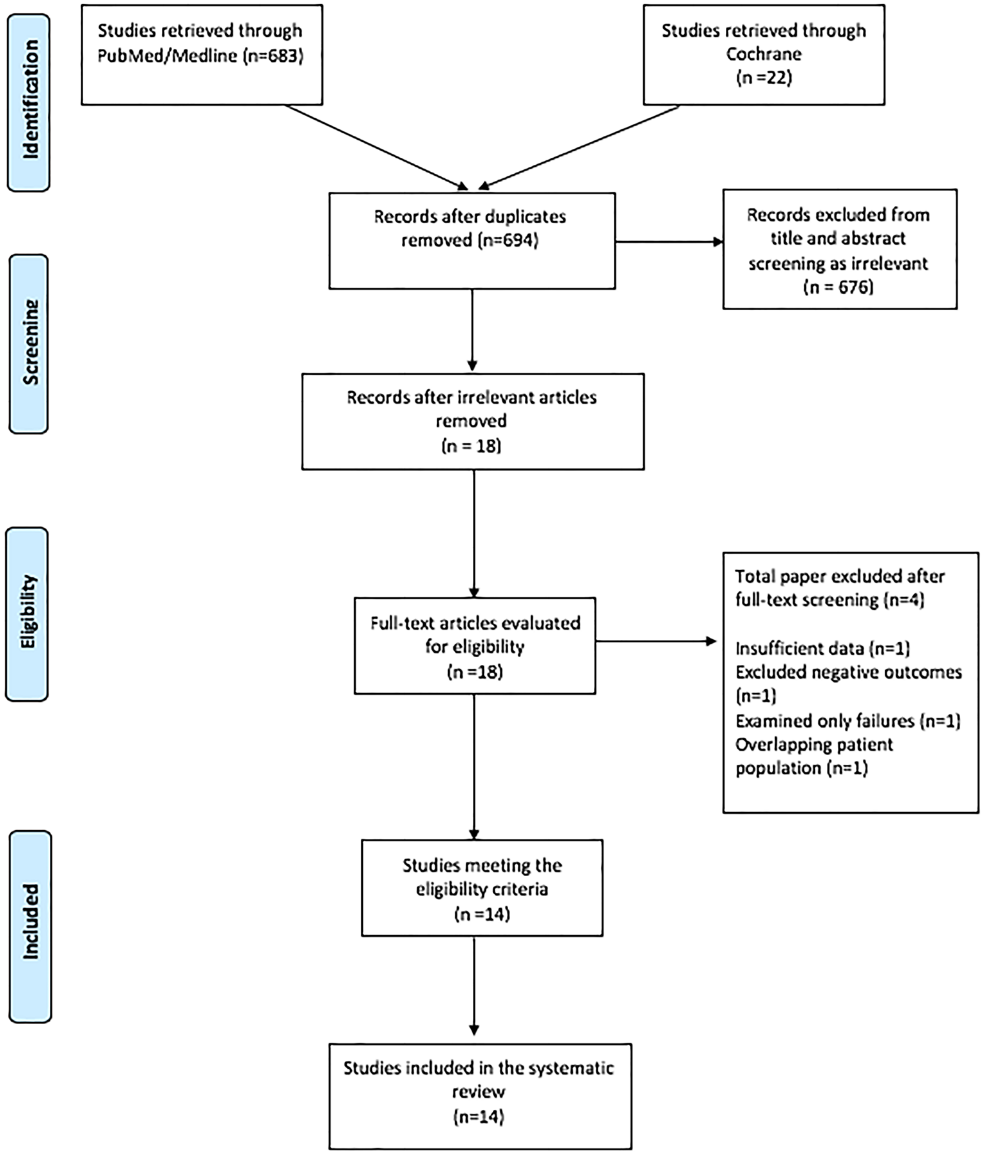

Fig. 1 PRISMA search flow diagram

19–28] Thirteen studies were observational and one was an RCT. None of the included observational studies or the sole RCT were assessed as having high risk of bias. A detailed assessment of risk of bias is available in the Supplemental Tables 1 and 2. Three of the included studies compared the combined ETV/CPC vs shunt approach while the rest compared ETV vs shunt. Five studies were conducted in Europe, four in Africa, four in USA/Canada, and one was international. Pertinent patient and study characteristics are presented in Table 1.

Post-operative outcomes for ETV ± CPC vs shunt

Pediatric patients who had an ETV (with or without CPC) were at a statistically significant lower risk of procedure-related infection compared to shunt (ETV: 1/300 (0.33%); shunt: 35/389 (8.9%)) (OR: 0.19; 95% CI: 0.07–0.53; I^2: 0%) (Fig. 2). There were no differences between patients in the ETV (43.4%, $N = 864/1989$) vs shunt groups (39.6% $N = 2496/6295$) (OR: 0.72; 95% CI: 0.39–1.32; I^2: 93.5%) in terms of re-operation (Fig. 3). The funnel plot for re-operation demonstrated asymmetry and the Egger's regression test ($p = 0.033$) validated that there is a high risk of publication bias for this outcome. (Supplemental Fig. 1). During the follow-up, all-cause mortality was reported in 4.5% ($N = 12/262$) and 8.5% ($N = 38/447$) of patients in the ETV and shunt groups, respectively; however statistical significance was not reached (OR: 0.77; 95% CI: 0.35–1.68; I^2: 0%) (Fig. 4). The incidence of post-procedural CSF leak was similar between the ETV (5.8%; $N = 10/172$) and shunt groups (3.2%; $N = 3/94$) (OR: 1.53; 95%

Table 1 Baseline patient and study characteristics

Study	Country	Years of enrollment	Arms	Shunt type	*N* (ETV/shunt)	Hydrocephalus etiology	Male %	Age (months)	Follow-up (months)
Cairo 2018	Democratic Republic of Congo	2003–2016	ETV/CPS vs VPS	VPS	(3/116)	Congenital Infection MMC	47.1	Avg 13.6 ± 22.7	3
Uche 2018	Nigeria	NR	ETV vs VPS	VPS	(25/30)	Congenital Cyst	67.3	Avg 27.6 ± 8.4	Avg 15.24 ± 2.28
Beuriat 2017	France	1985–1995	ETV vs VPS	VPS	(280/693)	Congenital Inflammatory Tumor	54.7	Avg 38.4 Med 6.4	12
Kulkarni 2017	Uganda	2013	ETV/CPC vs VPS	VPS	(43/57)	Infectious	61.0	Med 3.1 IQR 2.6–4.1	12
Pan 2017	USA	2003–2011	ETV vs Shunt	VPS Other	(455/455)	Congenital Infection IVH MMC Trauma Tumor	NR	Avg 102 ± 6.53	3
Beuriat 2016	France	1994–2012	ETV/CPC vs VPS	VPS	(32/18)	MMC	NR	Avg 0.77 Med 0.3 Range 0.03–7.53	Avg 103
Kulkarni 2016	International	2004–2013	ETV vs VPS	VPS	(115/43)	AS	NR	Med 3.6 IQR 1.6–6.6	Med 24.6 IQR 2.3–51.76
Paulsen 2016	Norway	2009–2013	ETV vs Shunt	VPS LPS VAS Other	(31/103)	AS Congenital Infection IVH & Other Hem. Tumor Unknown	60.4	Avg 47 Med 14 Range 0.03–180	24
Jernigan 2014	United States	2004–2009	ETV vs Shunt	VPS VAS Other	(872/4544)	Congenital CH NCH	55.7	Med 1.23 IQR 0.37–4.07	12
El-Ghandour 2010	Egypt	2003–2009	ETV vs VPS	VPS	(32/21)	Tumor	56.6	Avg 78 Range 24–144	ETV: Avg 27.4 ± 20.5 VPS: Avg 25 ± 19.7
Appelgren 2010	Sweden	2001–2005	ETV vs VPS	VPS	(22/76)	AS Congenital Cyst Infection IVH MMC Tumor	NR	VPS: Med 1.5 ETV: Med 21.6	56.4 27.6–96
De Ribaupierre 2007	Switzerland	1990–2004	ETV vs VPS	VPS	(24/31)	AS PF-L T/T-L Other	NR	Avg 55.2 Med 8.8 Range 12–204	Avg 52.8 Med 39

Table 1 (continued)

Study	Country	Years of enrollment	Arms	Shunt type	*N* (ETV/shunt)	Hydrocephalus etiology	Male %	Age (months)	Follow-up (months)
Garton 2002	Canada	1989–1998	ETV vs Shunt	–	(28/28)	AS MMC Tumors	NR	Avg 71.37 ± 68.90	Med 34.7 Range 2.9–72
Tuli 1999	Canada	1987–1996	ETV vs Shunt	–	(32/210)	AS Tumor	59.1	Med 43.2 Range 8.25–211.2	12

AS aqueductal stenosis, *CH* communicating hydrocephalus, *Hem.* hemorrhagic, *IVH* intraventricular hemorrhage, *MMC* meningiomyelocele, *NCH* non-communicating hydrocephalus, *NR* not reported, *ETV* endoscopic third ventriculostomy, *CPC* choroid plexus coagulation, *VPS* ventriculoperitoneal shunt

CI: 0.37–6.31; I^2: 0%) (Fig. 5). Shunt malfunction of any type was reported in 34.7% of the patients ($N = 331/954$).

Subgroup analyses for ETV/CPC and ETV only

Subgroup analyses for infection showed that ETV/CPC studies were not associated with a statistically significant lower risk for infection compared to shunt (OR: 0.32; 95% CI: 0.04–2.38; I^2: 23.9%) whereas ETV only studies showed a statistically significant lower risk of procedure-related infection (OR: 0.15; 95% CI: 0.04–0.52; I^2: 0%) (Supplemental Fig. 2). Subgroup analyses for the other outcomes were consistent with the pooled effect estimate and were not presented.

Subgroup analyses based on the geographic region

A subgroup analysis of re-operation based on the geographic region of the patients identified that ETV was associated with statistically significant lower odds to undergo any repeat procedure compared to shunt in studies conducted in Europe (OR: 0.39; 95% CI: 0.30–0.52; I^2: 1.4%) and Africa (OR: 0.13; 95% CI: 0.03–0.48; I^2: 0%) (Fig. 6). Studies conducted in USA/Canada did not show differences between the study groups and were accompanied by a significant amount of heterogeneity (OR: 1.49; 95% CI: 0.85–2.63; I^2: 86.2%) (Fig. 6). One study was international and was not included in any of the subgroups. The sole RCT was not included in the African subgroup as it would be inappropriate to be pooled with the other observational studies (see "Discussion").

Subgroup analyses for obstructive hydrocephalus cases only

The subgroup analysis of studies including only obstructive hydrocephalus cases showed that re-operation rates were 27.6% and 40.2% in the ETV and shunt groups, respectively; however, statistical significance was not reached (OR: 0.55; 95% CI: 0.24–1.25; I^2: 66.4%) (Fig. 7). Patients with obstructive hydrocephalus in the ETV group had statistically significant lower odds for infection as compared to the shunt group (OR: 0.14; 95% CI: 0.04–0.58; I^2: 0%) (Supplemental Fig. 3). No differences were identified in terms of all-cause mortality between the two groups (OR: 0.34; 95% CI: 0.09–1.34; I^2: 0%) (Supplemental Fig. 4).

Meta-regression analysis

Meta-regression analysis suggested that there is no statistically significant effect of the length of follow-up (coefficient: −0.003; 95%CI: −0.015–0.009, $p = 0.57$) (Supplemental Fig. 5) and average age (coefficient: −0.027; 95%CI: −0.011–0.006, $p = 0.50$) (Supplemental Fig. 6) of the patient population on the pooled estimate of re-operation. This

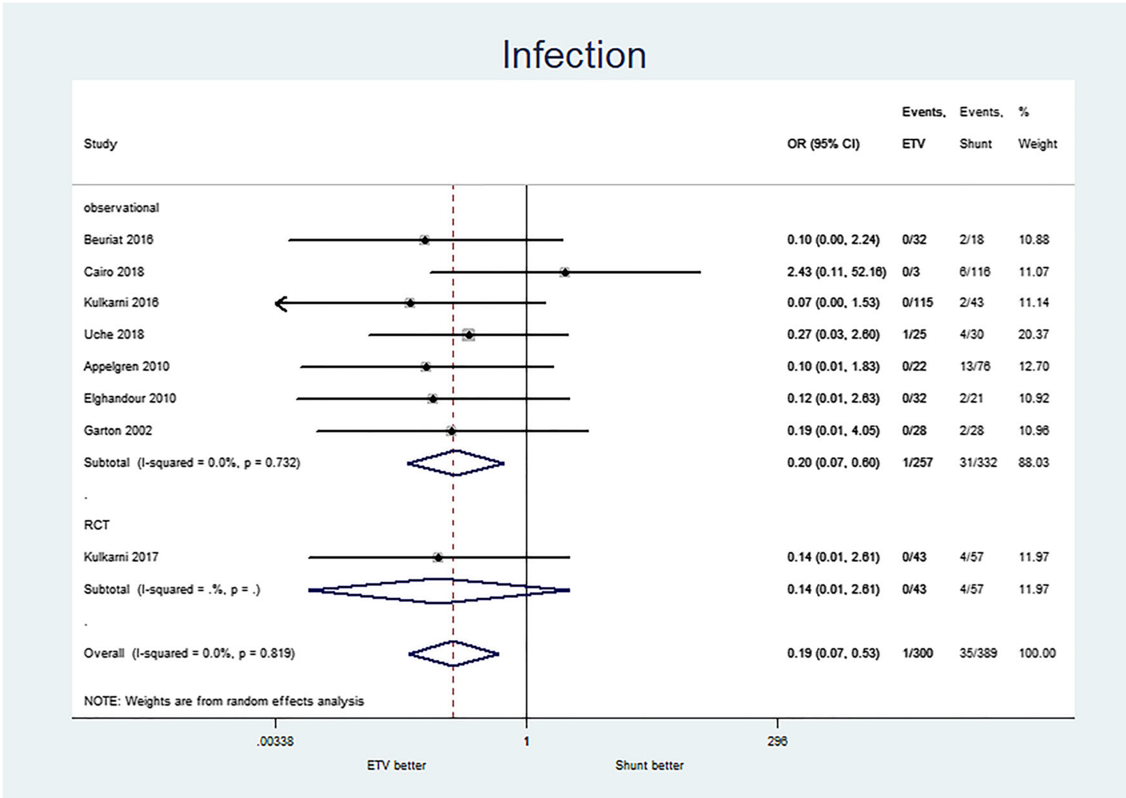

Fig. 2 Forest plot comparing post-operative infection in ETV vs shunt

suggests that these variables were not significant sources of heterogeneity.

Discussion

This meta-analysis included 8419 patients and evaluated the comparative efficacy of ETV vs shunt. Our results showed that patients who had ETV were at a statistically significant lower risk of any procedural-related infection, which was consistent in the subgroup analysis of obstructive hydrocephalus cases only. No differences in terms of repeat operations, mortality, and CSF leak were identified between the two groups in the original pooled analyses. Interestingly, ETV patients in Africa and Europe had significantly lower odds to undergo a re-operation than shunt patients whereas no difference was identified for patients in the USA/Canada.

Even though VPS has been used for several decades, it still remains associated with multiple complications including procedure-related infections, CSF leaks, a high failure, and re-operation rate and even mortality. [1] When ETV was introduced as an attractive alternative of shunting, its use was initially restricted to hydrocephalus caused by aqueductal stenosis; however, its indications are rapidly expanding. This was also reflected in the ETV indications reported in the included studies of this meta-analysis, including obstructive and non-obstructive hydrocephalus cases. [3, 29] ETV and shunting can be used for overlapping indications but a number of individual variables can predict procedural success and influence patient selection. Because of this, the choice of ETV and shunt is not always a simple binary argument of one versus the other. We therefore, caution the reader from interpreting the results of the present study to conclude that one procedure is simply superior to the other.

One of the most important complications in CSF diversion procedures is infections. [20] Despite significant efforts from organizations such as Hydrocephalus Clinical Research Network (HCRN), shunt infection remains a major source of morbidity and mortality. [30] The current meta-analysis demonstrated that ETV is associated with a statistically significant lower risk of procedure-related infection compared to shunting, during the follow-up. Interestingly, none of the individual studies reporting on this comparison showed statistically significant differences between ETV and shunt. It is likely that these studies were underpowered to detect this difference; however, meta-analytic methods increased the statistical power substantially, and therefore, statistical significance was reached. The pooled analysis including ETV plus or minus CPC and the subgroup analysis of ETV alone vs. shunt showed statistically significant lower odds of infection when ETV was used. However, the subgroup analysis of ETV + CPC vs shunt did not reach statistical significance. This could

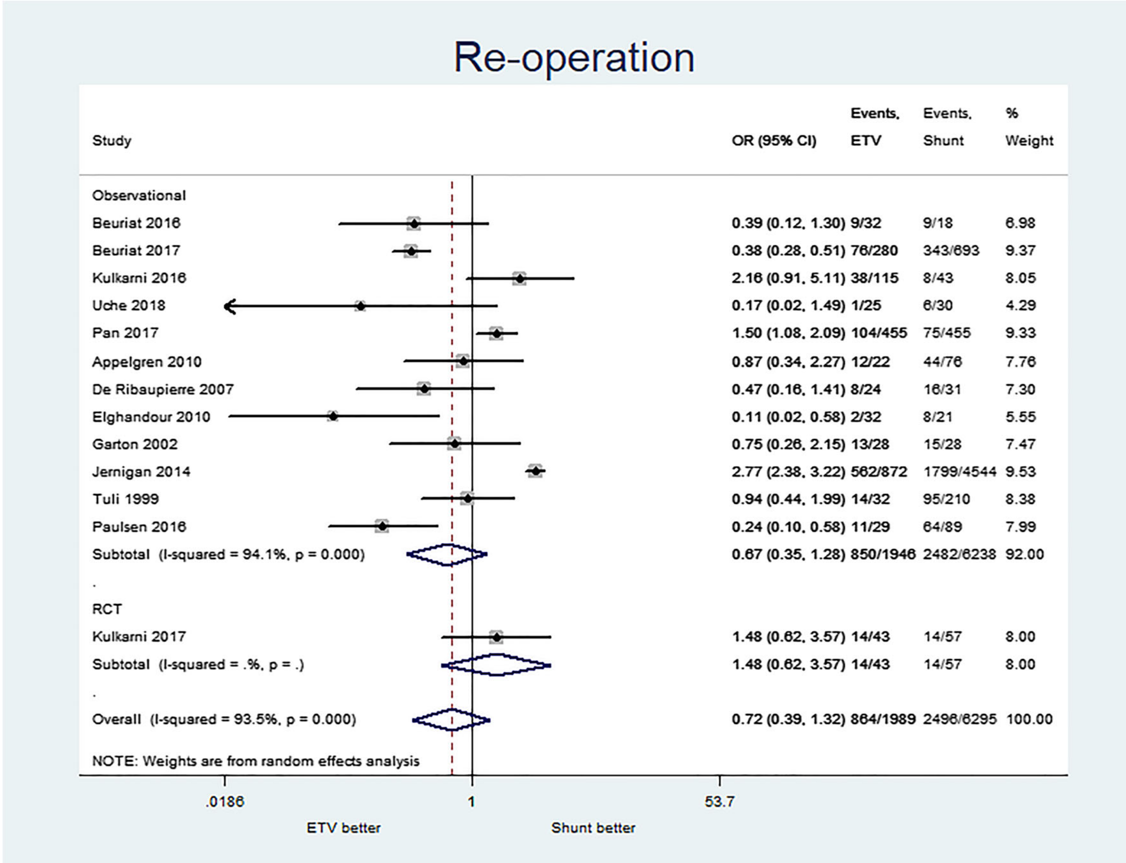

Fig. 3 Forest plot comparing re-operation rates in ETV vs shunt

be explained by a lack of statistical power in this subgroup analysis, as the absolute rates of infection were still lower in the ETV + CPC group as compared to shunt (Supplemental Fig. 2). Importantly, even though several studies have suggested that the up-front costs of shunting and ETV are similar, the average cost of admission due to shunt infection was $83,649. [27, 31] Future studies should investigate the potential long-term cost effectiveness of ETV compared to shunting by accounting for the cost of infections and re-operations needed in each group.

In cases where the primary CSF diversion procedure fails, a second surgery (either repeat of the first or use of an alternative modality) is commonly needed. [3, 32] In the studies included in our analysis, the specific type of second surgery was inconsistently reported. Our pooled analysis did not show any significant differences between ETV vs. shunt in terms of re-operation, but notably, this analysis was accompanied by a significant amount of heterogeneity (I^2: 94.2%). The heterogeneity prompted a subgroup analysis of re-operation based on the Continent in which the procedures were performed. Re-operation following ETV was 49.9% ($N = 693/1387$) in USA/Canada, 29.9% ($N = 116/387$) in Europe, and 5.2% in Africa ($N = 3/57$). However, re-operation rates following shunt were 37.8% ($N = 1984/5237$) in USA/Canada, 52.4% ($N = 476/907$) in Europe, and 27.4% ($N = 14/51$) in Africa. Furthermore, the subgroups of patients in Europe and Africa not only showed statistically significant lower re-operation rates in the ETV group, but also demonstrated a major reduction in heterogeneity ($I^2 = 1.4\%$ and $I^2 = 0\%$, respectively) as compared to the pooled analysis ($I^2 = 93.4\%$). In contrast, USA/Canada studies demonstrated the trend that shunt is associated with fewer re-operations; however, statistical significance was not reached. This is in line with a large prospective study by the HCRN which showed that ETV/CPC appears to be associated with a higher failure rate as compared to shunting. [33]

One possible explanation could be that studies conducted in the USA/Canada had shorter follow-up intervals compared to European or African, thus shunt cases did not have adequate time to develop complications and need re-operation. The two studies on patients in Africa had a follow-up of approximately 1 and 2 years, whereas the European studies reported a mean follow-up that ranged between 1 and 8 years. In contrast, the USA/Canada studies had a follow-up that ranged between 3 months and 3 years. Nevertheless, results from the meta-regression analysis showed that the duration of follow-up did not affect the size estimate of re-operation in the included studies. Another explanation may infer heterogeneities

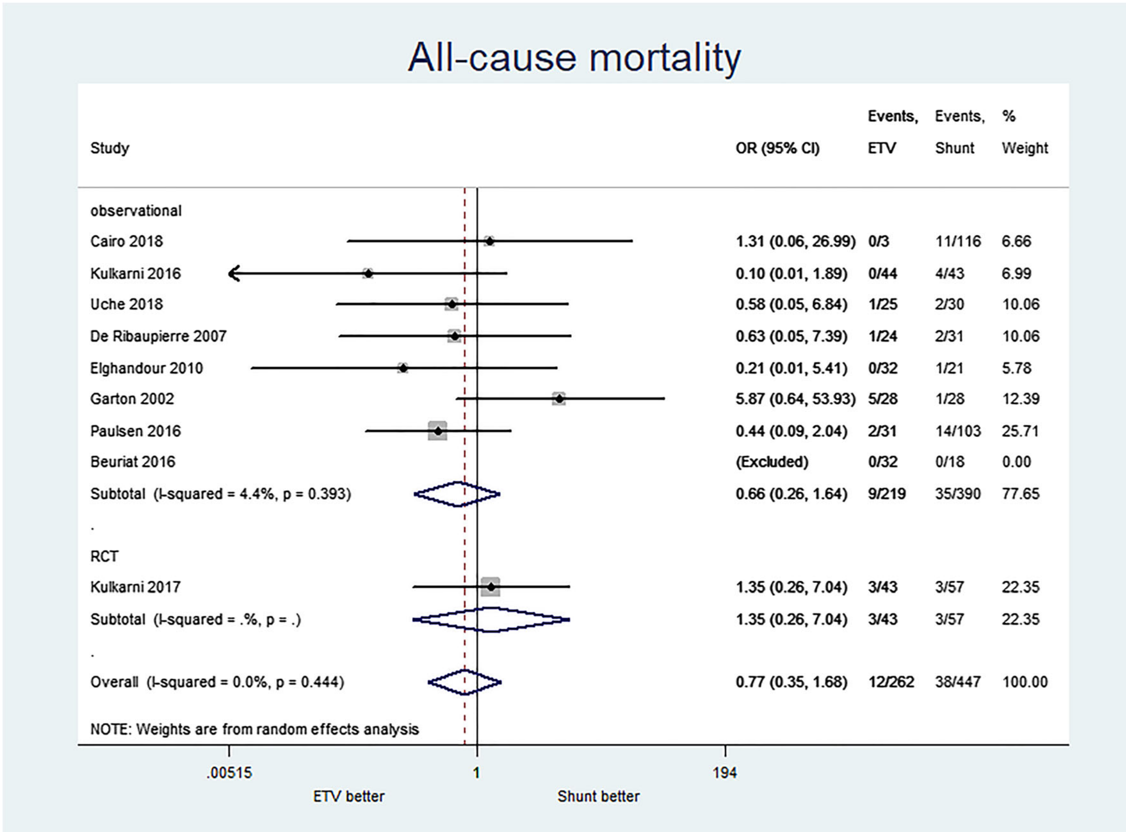

Fig. 4 Forest plot comparing all-cause mortality in ETV vs shunt

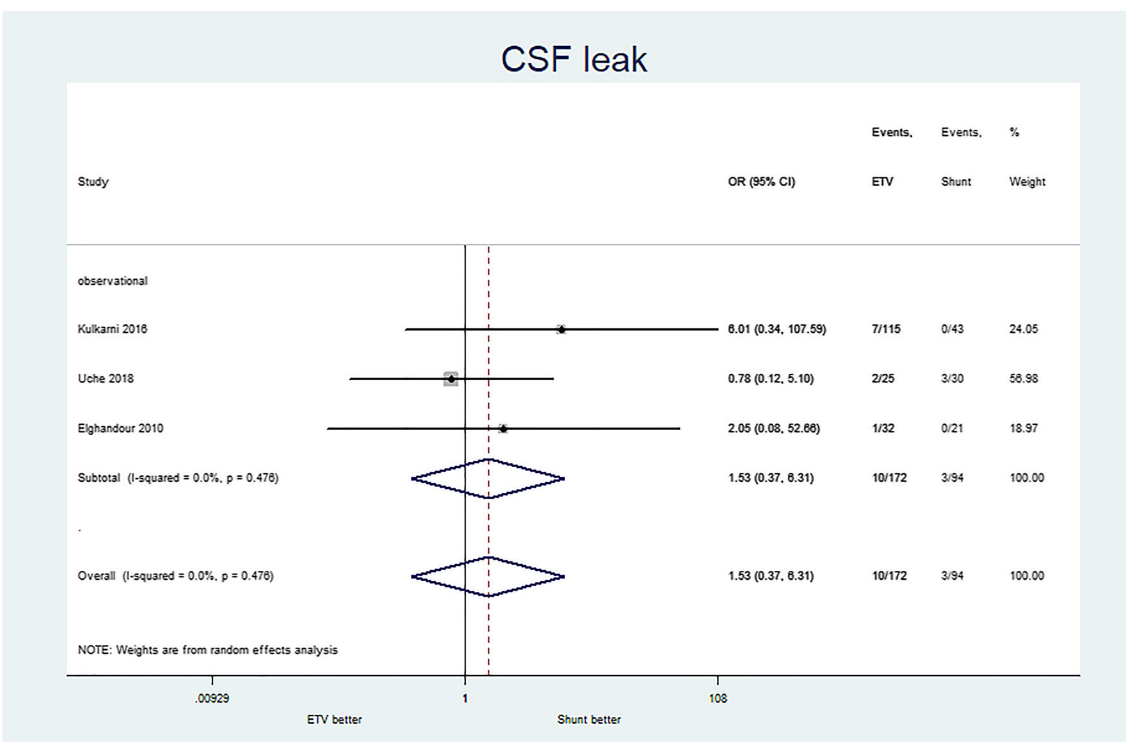

Fig. 5 Forest plot comparing cerebrospinal fluid (CSF) leak in ETV vs shunt

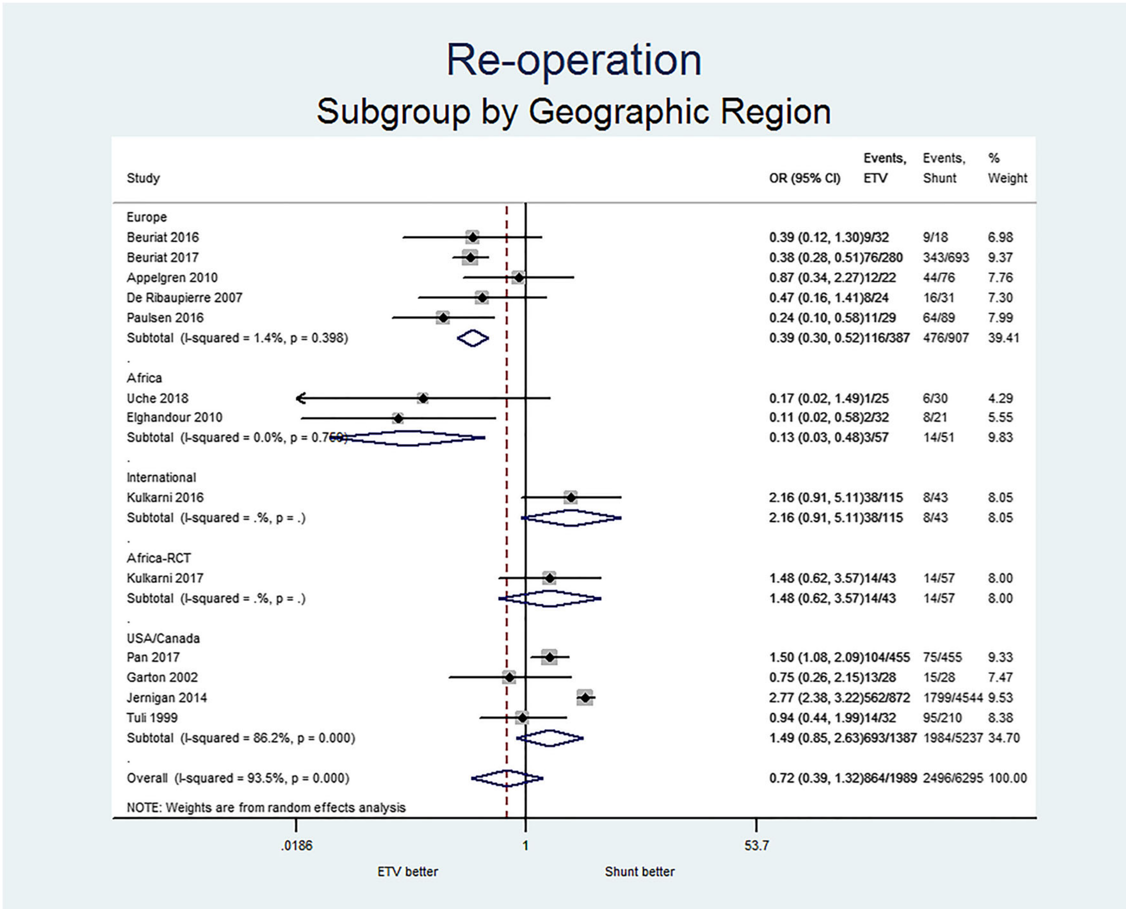

Fig. 6 Subgroup analysis of re-operation for ETV and shunt divided by the geographic region

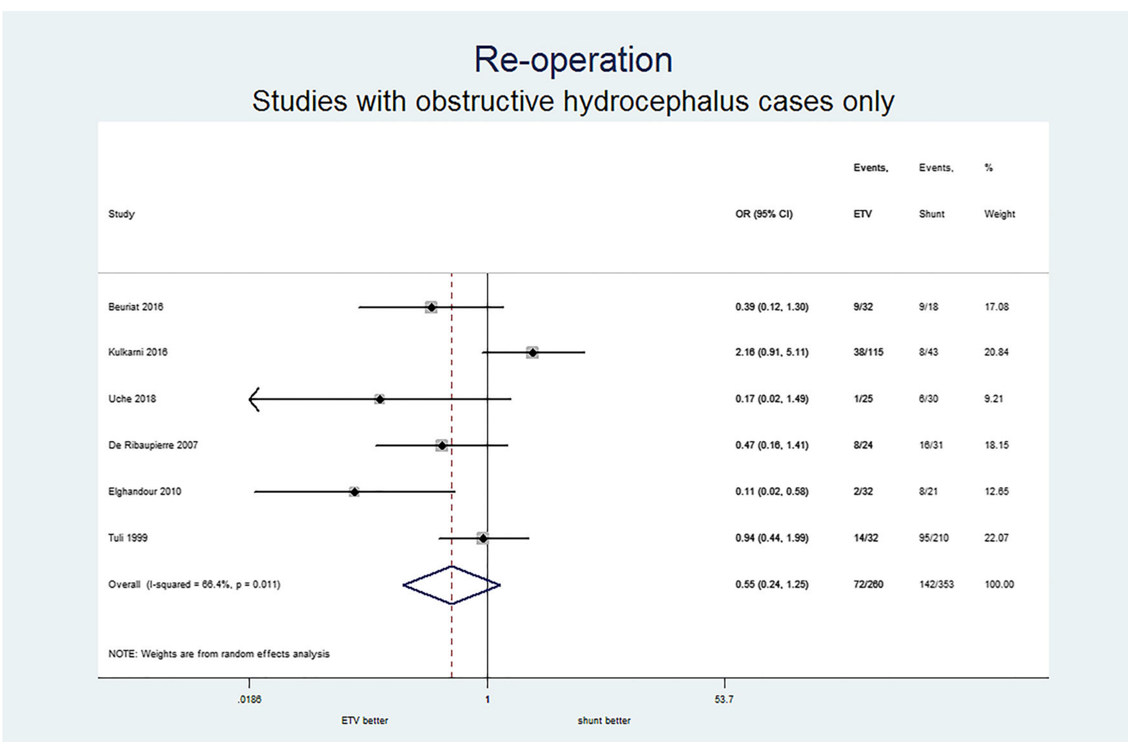

Fig. 7 Subgroup analysis of re-operation for ETV and shunt including only obstructive hydrocephalus cases

in shunt instrumentation, including valve types, catheters, anti-siphon devices, tip placement, and other technical considerations of the shunt or ETV approaches themselves. These details were inconsistently reported among the included studies. Lastly, perhaps most importantly, socioeconomic and cultural differences in availability of acute and emergent care capacities and attitudes toward repeat operations would have influenced clinicians in deciding performing ETV versus shunt.

It should be noted that three studies overall were conducted in Africa. Two of them were retrospective and when pooled, showed that ETV was associated with significantly lower odds of re-operation. The third study was a randomized trial and was not pooled with the two others, owing to the fundamental differences in their designs (randomized vs. observational). [34] In addition, even though this RCT was conducted in Africa, it was performed by North American investigators whereas the other African studies were performed by African investigators. Moreover, the RCT included only non-obstructive hydrocephalus cases for which the efficacy of ETV has been questioned. [9, 10, 14] In contrast, the two observational African studies included only obstructive hydrocephalus cases for which ETV efficacy has been well-documented. Due to these fundamental differences, the authors did not elect to pool the three African studies together.

The current study suggests that all-cause mortality and CSF leak rates are similar between the ETV and shunt groups. Our results are in agreement with the sole RCT by Kulkarni et al. who did not show any statistically significant differences between the study groups in terms of all-cause mortality. CSF leak was not reported by this RCT but was consistent with all included studies that synthesized this outcome. Future RCTs are warranted to validate the results of this study. In particular, future studies would benefit from standardized outcomes definitions for success and failure of ETV or shunt, uniform age and hydrocephalus etiology subgroups, and a predetermined long-term follow-up.

Limitations

Results of this study should be interpreted in the context of several limitations. First, the majority of the studies were observational which have an inherent risk for confounding and selection bias. Second, the follow-up intervals varied among the studies; however, our meta-regression analysis showed that re-operation rates were not affected by the duration of the follow-up. Third, patient populations were heterogeneous across the studies. The age groups were variable, but meta-regression results showed that age did not affect re-operation rates. This suggests that age was not a significant source of heterogeneity. The etiology of hydrocephalus varied across the studies; however, we were able to conduct subgroup analyses for obstructive hydrocephalus cases only, which showed similar results to those of the pooled analyses. In the pooled analyses, ETV and ETV + CPC were combined. However, to eliminate bias associated with this combination, subgroup analyses were conducted. Lastly, the sample size in the African subgroup was small, which limits the generalizability of our results.

Conclusions

This study shows that ETV was associated with a statistically significant lower risk of procedure-related infection compared to shunt. All-cause mortality and CSF leak rates were similar between the study groups. Re-operation rates were similar between the study groups in the pooled analysis. Subgroup analysis, based on the geographic region that the studies were conducted, suggested that ETV is associated with statistically significant lower odds for re-operation in Europe and Africa, but not in USA/Canada. Future RCTs are needed to validate the results of this study.

Funding statement This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Compliance with ethical standards

Conflict of interest None.

References

1. Beuriat P-A, Puget S, Cinalli G, Blauwblomme T, Beccaria K, Zerah M, Sainte-Rose C (2017) Hydrocephalus treatment in children: long-term outcome in 975 consecutive patients. J Neurosurg Pediatr 20:10–18. https://doi.org/10.3171/2017.2.PEDS16491
2. Pople IK (2002) Hydrocephalus and shunts: what the neurologist should know. J Neurol Neurosurg Psychiatry 73(Suppl 1):i17–i22
3. Jernigan SC, Berry JG, Graham DA, Goumnerova L (2014) The comparative effectiveness of ventricular shunt placement versus endoscopic third ventriculostomy for initial treatment of hydrocephalus in infants. J Neurosurg Pediatr 13:295–300. https://doi.org/10.3171/2013.11.PEDS13138
4. Uche EO, Onyia E, Mezue UC, Okorie E, Ozor II, Chikani MC (2013) Determinants and outcomes of ventriculoperitoneal shunt infections in Enugu, Nigeria. Pediatr Neurosurg 49:75–80. https://doi.org/10.1159/000357384
5. Stein SC, Guo W (2008) Have we made progress in preventing shunt failure? A critical analysis. J Neurosurg Pediatr 1:40–47. https://doi.org/10.3171/PED-08/01/040
6. Kulkarni AV, Riva-Cambrin J, Butler J, Browd SR, Drake JM, Holubkov R, Kestle JRW, Limbrick DD, Simon TD, Tamber MS, Wellons JC, Whitehead WE (2013) Outcomes of CSF shunting in children: comparison of hydrocephalus clinical research network cohort with historical controls: clinical article. J Neurosurg Pediatr 12:334–338. https://doi.org/10.3171/2013.7.PEDS12637
7. Greitz D (2007) Paradigm shift in hydrocephalus research in legacy of Dandy's pioneering work: rationale for third ventriculostomy in

communicating hydrocephalus. Childs Nerv Syst 23:487–489. https://doi.org/10.1007/s00381-007-0303-z
8. Koch-Wiewrodt D, Wagner W (2006) Success and failure of endoscopic third ventriculostomy in young infants: are there different age distributions? Childs Nerv Syst 22:1537–1541. https://doi.org/10.1007/s00381-006-0191-7
9. Hopf NJ, Grunert P, Fries G, Resch KDM, Perneczky A (1999) Endoscopic third ventriculostomy: outcome analysis of 100 consecutive procedures. Neurosurgery 44:795–796
10. Cinalli G, Salazar C, Mallucci C et al (1998) The role of endoscopic third ventriculostomy in the management of shunt malfunction. Neurosurgery 43:1323–1329
11. Warf BC (2005) Comparison of endoscopic third ventriculostomy alone and combined with choroid plexus cauterization in infants younger than 1 year of age: a prospective study in 550 African children. J Neurosurg 103:475–481. https://doi.org/10.3171/ped.2005.103.6.0475
12. Warf BC, Tracy S, Mugamba J (2012) Long-term outcome for endoscopic third ventriculostomy alone or in combination with choroid plexus cauterization for congenital aqueductal stenosis in African infants. J Neurosurg Pediatr 10:108–111. https://doi.org/10.3171/2012.4.PEDS1253
13. Pan I-W, Harris DA, Luerssen TG, Lam SK (2017) Comparative effectiveness of surgical treatments for pediatric hydrocephalus. Neurosurgery 0:1–8. https://doi.org/10.1093/neuros/nyx440
14. Kulkarni AV, Schiff SJ, Mbabazi-Kabachelor E, Mugamba J, Ssenyonga P, Donnelly R, Levenbach J, Monga V, Peterson M, MacDonald M, Cherukuri V, Warf BC (2017) Endoscopic treatment versus shunting for infant hydrocephalus in Uganda. N Engl J Med 377:2456–2464. https://doi.org/10.1056/NEJMoa1707568
15. Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart LA, the PRISMA-P Group (2015) Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ 349:g7647
16. Sterne JA, Hernan MA, Reeves BC et al (2016) ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. BMJ 355:i4919
17. Higgins JPT, Altman DG, Gøtzsche PC et al (2011) The Cochrane collaboration's tool for assessing risk of bias in randomised trials. BMJ 343:d5928. https://doi.org/10.1136/bmj.d5928
18. Higgins JPT, Thompson SG, Deeks JJ, Altman DG (2003) Measuring inconsistency in meta-analyses. BMJ 327:557–560. https://doi.org/10.1136/bmj.327.7414.557
19. Cairo SB, Agyei J, Nyavandu K, Rothstein DH, Kalisya LM (2018) Neurosurgical management of hydrocephalus by a general surgeon in an extremely low resource setting: initial experience in north Kivu province of eastern Democratic Republic of Congo. Pediatr Surg Int 34:467–473. https://doi.org/10.1007/s00383-018-4238-0
20. Uche EO, Okorie C, Iloabachie I, Amuta DS, Uche NJ (2018) Endoscopic third ventriculostomy (ETV) and ventriculoperitoneal shunt (VPS) in non-communicating hydrocephalus (NCH): comparison of outcome profiles in Nigerian children. Childs Nerv Syst 34:1683–1689. https://doi.org/10.1007/s00381-018-3848-0
21. Beuriat P-A, Szathmari A, Grassiot B, Plaisant F, Rousselle C, Mottolese C (2016) Role of endoscopic third Ventriculostomy in the Management of Myelomeningocele-Related Hydrocephalus: a retrospective study in a single French institution. World Neurosurg 87:484–493. https://doi.org/10.1016/j.wneu.2015.07.071
22. Kulkarni AV (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 32:1039–1048. https://doi.org/10.1007/s00381-016-3095-1
23. Paulsen AH, Due-tønnessen BJ, Lundar T, Lindegaard K (2016) Cerebrospinal fluid (CSF) shunting and ventriculocisternostomy (ETV) in 400 pediatric patients . Shifts in understanding , diagnostics , case-mix , and surgical management during half a century. Childs Nerv Syst 33:1–10. https://doi.org/10.1007/s00381-016-3281-1
24. El-Ghandour NMF (2011) Endoscopic third ventriculostomy versus ventriculoperitoneal shunt in the treatment of obstructive hydrocephalus due to posterior fossa tumors in children. Childs Nerv Syst 27:117–126. https://doi.org/10.1007/s00381-010-1263-2
25. Appelgren T, Zetterstrand S, Elfversson J, Nilsson D (2010) Long-term outcome after treatment of hydrocephalus in children. Pediatr Neurosurg 46:221–226. https://doi.org/10.1159/000319365
26. de Ribaupierre S, Rilliet B, Vernet O, Regli L, Villemure JG (2007) Third ventriculostomy vs ventriculoperitoneal shunt in pediatric obstructive hydrocephalus: results from a Swiss series and literature review. Childs Nerv Syst 23:527–533. https://doi.org/10.1007/s00381-006-0283-4
27. Garton HJL, Kestle JRW, Cochrane DD, Steinbok P (2002) A cost-effectiveness analysis of endoscopic third ventriculostomy. Neurosurgery 51:68–69
28. Tuli S, Alshail E, Drake J (1999) Third ventriculostomy versus cerebrospinal fluid shunt as a first procedure in pediatric hydrocephalus. Pediatr Neurosurg 30:11–15. https://doi.org/10.1159/000028753
29. Pan I-W, Harris DA, Luerssen TG, Lam SK (2018) Comparative effectiveness of surgical treatments for pediatric hydrocephalus. Neurosurgery 83:480–487. https://doi.org/10.1093/neuros/nyx440
30. Kestle JRW, Holubkov R, Douglas Cochrane D, Kulkarni AV, Limbrick DD, Luerssen TG, Jerry Oakes W, Riva-Cambrin J, Rozzelle C, Simon TD, Walker ML, Wellons JC, Browd SR, Drake JM, Shannon CN, Tamber MS, Whitehead WE (2016) A new hydrocephalus clinical research network protocol to reduce cerebrospinal fluid shunt infection. J Neurosurg Pediatr 17:391–396. https://doi.org/10.3171/2015.8.PEDS15253
31. Pham ACQ, Fan C, Owler BK (2013) Treating pediatric hydrocephalus in Australia: a 3-year hospital-based cost analysis and comparison with other studies. J Neurosurg Pediatr 11:398–401. https://doi.org/10.3171/2013.1.PEDS12233
32. Li C, Gui S, Zhang Y (2017) Compare the safety and efficacy of endoscopic third ventriculostomy and ventriculoperitoneal shunt placement in infants and children with hydrocephalus: a systematic review and meta-analysis. Int J Neurosci:1–30. https://doi.org/10.1080/00207454.2017.1348352
33. Kulkarni AV, Riva-Cambrin J, Rozzelle CJ, Naftel RP, Alvey JS, Reeder RW, Holubkov R, Browd SR, Cochrane DD, Limbrick DD, Simon TD, Tamber M, Wellons JC, Whitehead WE, Kestle JRW (2018) Endoscopic third ventriculostomy and choroid plexus cauterization in infant hydrocephalus: a prospective study by the hydrocephalus clinical research network. J Neurosurg Pediatr 21:214–223. https://doi.org/10.3171/2017.8.PEDS17217
34. PT Higgins J, Green S (2009) Cochrane handbook for systematic reviews of interventions version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available from http://handbook.cochrane.org. Accessed 3/5/2019