Treatment of posthemorrhagic ventricular dilation in preterm infants: a systematic review and meta-analysis of outcomes and complications

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OBJECT The optimal clinical management of intraventricular hemorrhage (IVH) and posthemorrhagic ventricular dilation (PHVD)/posthemorrhagic hydrocephalus (PHH) in premature infants remains unclear. A common approach involves temporary treatment of hydrocephalus in these patients with a ventriculosubgaleal shunt (VSGS), ventricular access device (VAD), or external ventricular drain (EVD) until it becomes evident that the patient needs and can tolerate permanent CSF diversion (i.e., ventriculoperitoneal shunt). The present systematic review and meta-analysis aimed to provide a robust and comprehensive summary of the published literature regarding the clinical outcomes and complications of these 3 techniques as temporizing measures in the management of prematurity-related PHVD/PHH.

METHODS The authors searched MEDLINE, EMBASE, CINAHL, Google Scholar, and the Cochrane Library for studies published through December 2013 on the use of VSGSs, VADs, and/or EVDs as temporizing devices for the treatment of hydrocephalus following IVH in the premature neonate. Data pertaining to patient demographic data, study methods, interventions, and outcomes were extracted from eligible articles. For each of the 3 types of temporizing device, the authors performed meta-analyses examining 6 outcomes of interest, which were rates of 1) obstruction; 2) infection; 3) arrest of hydrocephalus (i.e., permanent shunt independence); 4) mortality; 5) good neurodevelopmental outcome; and 6) revision.

RESULTS Thirty-nine studies, representing 1502 patients, met eligibility criteria. All of the included articles were observational studies; 36 were retrospective and 3 were prospective designs. Nine studies (n = 295) examined VSGSs, 24 (n = 962) VADs, and 9 (n = 245) EVDs. Pooled rates of outcome for VSGS, VAD, and EVD, respectively, were 9.6%, 7.3%, and 6.8% for obstruction; 9.2%, 9.5%, and 6.7% for infection; 12.2%, 10.8%, and 47.3% for revision; 13.9%, 17.5%, and 31.8% for arrest of hydrocephalus; 12.1%, 15.3%, and 19.1% for death; and 58.7%, 50.1%, and 56.1% for good neurodevelopmental outcome.

CONCLUSIONS This study provides robust estimates of outcomes for the most common temporizing treatments for IVH in premature infants. With few exceptions, the range of outcomes was similar for VSGS, VAD, and EVD.

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KEY WORDS cerebrospinal fluid shunts; hydrocephalus; intraventricular hemorrhage; premature birth; vascular disorders

THE average incidence of preterm birth in 2010 was 11.1% globally and 12.0% in the US.⁹ Advances in fetal medicine and obstetric and neonatal intensive care over recent decades have improved the survival of premature infants born at ever-earlier gestational ages.^{4,62} This is perhaps one of the greatest successes of modern medicine, but one that has brought its fair share of chal-

lenges. Preterm infants are at risk for multiple comorbidities, including bronchopulmonary dysplasia, necrotizing enterocolitis, retinopathy of prematurity, among others.¹⁷ Greater survival among these patients has hence translated into increased burden of morbidity.⁶² Intraventricular hemorrhage (IVH) and posthemorrhagic ventricular dilation (PHVD) are complications of prematurity that portend

ABBREVIATIONS EVD = external ventricular drain; IVH = intraventricular hemorrhage; PHH = posthemorrhagic hydrocephalus; PHVD = posthemorrhagic ventricular dilation; VAD = ventricular access device; VSGS = ventriculosubgaleal shunt.

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considerable neurodevelopmental sequelae, including cognitive delay, visual impairment, behavioral abnormalities, epilepsy, cerebral palsy, and symptomatic hydrocephalus.^{1,27,57} It is estimated that 25%–30% of premature/low-birth-weight infants suffer from IVH.^{23,33} PHVD develops in 25%–50% of these neonates, and roughly 40% require some treatment for hydrocephalus.^{11,45,66}

Treatment paradigms for PHVD/posthemorrhagic hydrocephalus (PHH) in premature infants have shifted time and time again, and have included diuretics, serial lumbar puncture, intraventricular fibrinolytics, ventricular access device (VAD), external ventricular drain (EVD), and ventriculostomy (VSGS).⁵⁹ To date, there remains little in the way of evidence to guide the pediatric neurosurgeon. A common approach used today is to treat PHVD/PHH with a temporizing device—most commonly, either a VAD or VSGS, and less frequently, an EVD—until placement of a permanent ventriculoperitoneal shunt becomes a necessary and safe undertaking. The choice of temporizing measure remains a topic of heavy debate, and there have been few direct comparisons between the aforementioned methods. To that end, we undertook a systematic review and meta-analysis to provide the best estimates of various relevant outcomes of VSGS, VAD, and EVD in the management of prematurity-related PHVD/PHH.

Methods

This systematic review and meta-analysis was conducted in accordance with the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) guidelines⁶³ and the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement.⁴⁴

Search Strategy

We searched, without language restrictions, MEDLINE, EMBASE, CINAHL, Google Scholar, and the Cochrane Library from the start date of each source through December 2013. We looked for studies reporting clinical outcomes of the use of VSGS, VAD, and/or EVD as temporizing measures for the treatment of hydrocephalus following IVH in preterm infants. We used, in various combinations, keywords/MeSH terms related to prematurity (e.g., neonate, premature infant, prematurity, preterm infant); posthemorrhagic hydrocephalus (e.g., hydrocephalus, intracranial hemorrhage, intraventricular hemorrhage, ventricular dilation, ventriculomegaly); and pertinent methods of CSF diversion (e.g., cerebrospinal fluid shunt, McComb reservoir, Ommaya reservoir, Rickham reservoir, subgaleal shunt, ventricular access device, ventricular catheter, ventricular reservoir, ventriculostomy, ventriculostomy shunt). We also manually searched the references of relevant articles to identify additional studies for consideration.

Selection Criteria

Two authors (J.H.B. and C.J.H.) independently evaluated the studies for eligibility. The inclusion criteria were: 1) population, defined as premature infants with PHVD/PHH; 2) intervention, defined as VSGS, VAD, and/or EVD; and 3) outcome, defined as at least 1 of the follow-

ing: obstruction, infection, arrest of hydrocephalus, mortality, neurodevelopmental outcome, or revision. Cohorts with a sample size < 10 were excluded. For studies reporting data on overlapping cohorts from the same institution, we included only the study with the most inclusive cohort to prevent duplications. Abstracts from meeting proceedings were excluded if the data were not published as full-text articles in a peer-reviewed journal. Disagreements between the 2 reviewers concerning the decision to include or exclude a study were resolved by consensus and, if necessary, consultation with a third reviewer (A.V.K. or J.R.C.).

Data Extraction

From eligible reports, we abstracted data relating to patient characteristics, study methods, interventions, and outcomes. All data were independently extracted by the 2 primary reviewers, and verified for accuracy by the third reviewer. Discrepancies were resolved by discussion and consensus.

We abstracted the total number of events for 6 outcomes of interest: obstruction, infection, arrest of hydrocephalus, mortality, good neurodevelopmental outcome, and revision. Arrest of hydrocephalus was defined as children known, unequivocally, to be alive without having undergone permanent CSF diversion (i.e., shunt or endoscopic third ventriculostomy). Mortality included all deaths in patients who received a temporizing device (i.e., VSGS, VAD, or EVD), regardless of cause and need for permanent CSF diversion. Children with normal cognitive, language, social, and motor function, or only mild deficits in these functions, were considered to have a good developmental outcome. A revision was any operation for replacement, revision, or infection of a temporizing device.

Quality Assessment

Two reviewers performed quality assessment. We used the Newcastle-Ottawa Scale⁶⁷ to evaluate comparability, selection of cohort, and assessment of outcome among eligible studies.

Statistical Analyses

Cohorts were grouped based on treatment modality: VSGS, VAD, or EVD. Because there were too few studies that provided a direct comparison of outcomes between 2 or more of these interventions, we instead performed meta-analyses for each of the 6 outcomes of interest for each intervention separately. Obstruction, infection, arrest of hydrocephalus, mortality, and good neurodevelopmental outcome were expressed as proportions based on number of patients, whereas revision rates were calculated based on number of devices.

Between-study heterogeneity was evaluated by Cochran's *Q* test and measured by the *I*² statistic, with *I*² values exceeding 25%, 50%, and 75% representing low, moderate, and high heterogeneity, respectively.²⁴ The DerSimonian-Laird random effects model was used to calculate pooled proportions with 95% CIs. Weights were calculated by the inverse variance method. Publication bias was evaluated visually by funnel plot analysis and quantified by Begg and Mazumdar's⁸ and Egger's tests.¹⁶ The threshold Type

I error rate for statistical significance was set a priori at $\alpha = 0.05$ (2-tailed). We used Comprehensive Meta-Analysis version 2.2 (Biostat, Inc.) to conduct all statistical analyses.

Results

Our search yielded 1748 studies, of which 1591 were excluded after title and abstract screening (Fig. 1). An additional 118 resources were excluded following full-text review. The remaining 39 studies reporting on 1502 patients of interest were included in our systematic review and meta-analysis. There were 3 prospective observational studies; the remaining 36 studies were retrospective designs.

Ventriculosubgaleal Shunt

Nine studies ($n = 295$) examined VSGSs (Table 1). Pooled rates of outcome were 9.6% (95% CI 5.6–16.0) for obstruction, 9.2% (95% CI 6.3–13.3) for infection, 13.9% (95% CI 9.6–19.8) for arrest of hydrocephalus, 12.1% (95% CI 5.3–25.3) for mortality, 58.7% (95% CI 26.8–84.6) for good neurodevelopmental outcome, and 12.2% (95% CI 8.8–16.5) for revision (Fig. 2).

Ventricular Access Device

Twenty-four studies ($n = 962$) reported on the use of VADs (Table 2). Summary estimates were 7.3% (95% CI 5.0–10.4) for obstruction, 9.5% (95% CI 7.0–12.8) for infection, 17.5% (95% CI 13.0–23.2) for arrest of hydrocephalus, 15.3% (95% CI 10.4–22.0) for mortality, 50.1% (95% CI 34.3–65.8) for good neurodevelopmental outcome, and 10.8% (95% CI 7.4–15.5) for operative revision (Fig. 3).

External Ventricular Drain

Nine reports ($n = 245$) used EVDs to temporize PHVD in premature neonates (Table 3). Pooled event rates were 6.8% (95% CI 3.3–13.5) for obstruction, 6.7% (95% CI 3.9–11.1) for infection, 31.8% (95% CI 21.7–43.9) for arrest of hydrocephalus, 19.1% (95% CI 14.2–25.3) for mortality, 56.1% (95% CI 34.8–75.4) for good neurodevelopmental

FIG. 1. A flowchart summarizing the literature search and study selection process.

TABLE 1. Included studies using VSGS as a temporizing measure in prematurity-related PHVD/PHH

Authors & Year	No. of Pts	Sex (M/F)	Pt Characteristics		No. of Pts (%) w/ Outcome					
			Mean GA (wks)	Mean BW (g)	IVH Grade (Papile)	Obstruction	Infection	Arrest of Hydrocephalus	Death	Good Neurodevelopmental Outcome
Sklar et al., 1992	62						6 (9.7)	6 (9.7)	7 (11.3)	17/54 (31.5)
Rahman et al., 1995	15	9:6	29	1284	II, $n = 1$; III, $n = 8$; IV, $n = 6$	0 (0)	0 (0)	3 (20.0)	0 (0)	12 (80.0)
Karas et al., 2007	17	12:5	26			2 (11.8)	0 (0)	0 (0)	0 (0)	2/19 (10.5)
Lam & Heilman, 2009	16*	9:7	27.4	998	III, $n = 9$; IV, $n = 7$	3 (18.8)	1 (6.3)	4 (25.0)	2 (12.5)	4/20 (20.0)
Wellons et al., 2009	36†				III or IV		5 (13.9)			
Köksal & Oktem, 2010	25	8:17	29.2	1342	II, $n = 8$; III, $n = 13$; IV, $n = 4$		2 (8.0)	3 (12.0)	13 (52.0)	12/18 (66.7)
Limbrick et al., 2010	30‡		27.6		III or IV		1 (3.3)	7 (23.3)	4 (13.3)	3/33 (9.1)
Alan et al., 2012	22		26.6	985		2 (9.1)	3 (13.6)	3 (13.6)	3 (13.6)	3/25 (12.0)
Nagy et al., 2013	72		27.3	1037		5 (6.9)	6 (8.3)	6 (8.3)	3 (4.2)	11/83 (13.3)

BW = birth weight; GA = gestational age; pts = patients.

* Lam & Heilman, 2009: $N = 32$ (16 patients received VSGS; 16 received VAD).

† Wellons et al., 2009: $N = 124$ (36 patients received VSGS; 88 received VAD).

‡ Limbrick et al., 2010: $N = 95$ (30 patients received VSGS; 65 received VAD).

FIG. 2. Forest plots of meta-analyses of outcomes and complications of VSGS for treatment of PHVD in preterm infants. Obstruction (A); infection (B); arrest of hydrocephalus (C); death (D); good neurodevelopmental outcome (E); and revision (F).

TABLE 2. Included studies using VAD as a temporizing measure in prematurity-related PHVD/PHH

Authors & Year	No. of Pts	Sex (M/F)	Pt Characteristics			No. of Pts (%) w/ Outcome				
			Mean GA (wks)	Mean BW (g)	IVH Grade (Papile)	Obstruction	Infection	Arrest of Hydrocephalus	Death	Good Neurodevelopmental Outcome
Marlin, 1980	12		29.3	1215				1 (8.3)	7 (58.3)	2/12 (16.7)
Anwar et al., 1986	19	10:9	28	1045	III, n = 11; IV, n = 8	2 (10.5)	2 (10.5)	3 (15.8)	3 (15.8)	3/5 (60.0)
Gaskill et al., 1988	38				III or IV		0 (0)	4 (10.5)	11 (28.9)	5/29 (17.2)
Brockmeyer et al., 1989	20	11:9	27.7	1041	III, n = 5; IV, n = 15		2 (10.0)	4 (20.0)	4 (20.0)	10/14 (71.4)
Leonhardt et al., 1989	13		29	1070	II-IV	0 (0)	0 (0)	1 (7.7)	0 (0)	1/14 (7.1)
Levy et al., 1997	72	46:26	29	1187	III or IV	1 (1.4)	2 (2.8)	6 (8.3)	31 (43.1)	17/41 (41.5)
Hudgins et al., 1998	149	91:58	26.3	994	I, n = 3; II, n = 8; III, n = 62; IV, n = 76	15 (10.1)	12 (8.1)	16 (10.7)	16 (10.7)	22/180 (12.2)
Heep et al., 2001	20	14:6	26.7	1135	III or IV		1 (5.0)	3 (15.0)	0 (0)	3/20 (15.0)
Richard et al., 2001	64	39:25	29.2	1318	II, n = 2; III, n = 58; IV, n = 4	4 (6.3)	14 (21.9)	14 (21.9)	19 (29.7)	26/43 (60.5)
de Vries et al., 2002	29				III		7 (24.1)	10 (34.5)	0 (0)	
Murphy et al., 2002	12							1 (8.3)	1 (8.3)	
Futagi et al., 2005	17*		30.3	1448	III or IV		1 (5.9)	0 (0)	2 (11.8)	
Brouwer et al., 2008	76	36:40	30.2	1473			7 (9.2)			11/83 (13.3)
Peretta et al., 2007	18	13:5	29.8	1313	II, n = 1; III, n = 5; IV, n = 12	1 (5.6)	1 (5.6)	3 (16.7)	1 (5.6)	2/19 (10.5)
Lam & Heilman, 2009	16†	9:7	29.2	1279	III, n = 9; IV, n = 7	1 (6.3)	0 (0)	1 (6.3)	0 (0)	1/17 (5.9)
Wellons et al., 2009	88‡				III or IV		11 (12.5)			
Yu et al., 2009	11		29	1467	III		0 (0)	6 (54.5)	1 (9.1)	
Kormanik et al., 2010	29	17:12	26.9	1070	II, n = 3; III, n = 11; IV, n = 15		1 (3.4)	3 (10.3)	3 (10.3)	1/29 (3.4)
Limbrick et al., 2010	65§		27.6		III or IV	2 (3.1)	4 (6.2)	15 (23.1)	4 (6.2)	2/67 (3.0)
Bajaj et al., 2012	52		26	796	I/II, n = 6; III/IV, n = 46		5 (9.6)		6 (11.5)	
Tian et al., 2012	27	18:9	28	1255	III or IV	1 (3.7)	0 (0)	6 (22.2)	2 (7.4)	3/30 (10.0)
Chittiboina et al., 2013	65		27.1	1001					9 (13.8)	
Ma et al., 2013	20									
Mihajlovic et al., 2013	30		29.3				2 (10.0)	8 (40.0)	9 (30.0)	18/30 (60.0)

* Futagi et al., 2005: N = 21 (17 patients received VAD; 4 received EVD).

† Lam & Heilman, 2009: N = 32 (16 patients received VAD; 16 received VSGS).

‡ Wellons et al., 2009: N = 124 (88 patients received VAD; 36 received VSGS).

§ Limbrick et al., 2010: N = 95 (65 patients received VAD; 30 received VSGS).

FIG. 3. Forest plots of meta-analyses of outcomes and complications of VAD for treatment of PHVD in preterm infants. Obstruction (A); infection (B); arrest of hydrocephalus (C); death (D); good neurodevelopmental outcome (E); and revision (F).

outcome, and 47.3% (95% CI 29.7–65.7) for surgical revision (Fig. 4).

Discussion

Our study aimed to provide a synthesis of the available evidence concerning the use of VSGSs, VADs, and EVDs

as temporizing devices for PHVD/PHH in preterm infants. We conducted a comprehensive search of the world literature and determined pooled summary estimates for several outcomes of interest. The greatest limitation of our study, as with most meta-analyses, is heterogeneity, for which there are many causes. The baseline populations in the primary studies probably differed in many ways,

TABLE 3. Included studies using EVD as a temporizing measure in prematurity-related PHVD/PHH

Authors & Year	Patient Characteristics				No. of Pts (%) w/ Outcome						
	No. of Pts	Sex (M/F)	Mean GA (wks)	Mean BW (g)	IVH Grade (Papile)	Obstruction	Infection	Hydrocephalus	Arrest of Death	Good Neurodevelopmental Outcome	Revision
Allan et al., 1982	10						1 (10.0)	7 (70.0)	0 (0)		
Kreusser et al., 1984	19		30.8	1363	II, n = 9; III, n = 10		2 (10.5)	3 (15.8)	3 (15.8)	4/16 (25.0)	19/38 (50.0)
Rhodes et al., 1987	37	28:9	29.3	1236	II, n = 10; III, n = 4; IV, n = 23		4 (10.8)	10 (27.0)	10 (27.0)	21/27 (77.8)	43/66 (65.2)
Marro et al., 1991	24		29	1310	I, n = 5; II/III, n = 11; IV, n = 8		1 (4.2)	9 (37.5)	3 (12.5)		57/70 (81.4)
Massone et al., 1994	21		29.6	1443	III, n = 11; IV, n = 10	0 (0)	1 (4.8)	11 (52.4)	3 (14.3)		0/21 (0)
Cornips et al., 1997	14	5:9	29	1273	III, n = 10; IV, n = 4	0 (0)	0 (0)	5 (35.7)	0 (0)	7/14 (50.0)	10/24 (41.7)
Reinprecht et al., 2001	76		29.8	1364	II, n = 4; III, n = 38; IV, n = 21; NA, n = 13	6 (7.9)	2 (2.6)	22 (28.9)	15 (19.7)	25/39 (64.1)	36/112 (32.1)
Olischar et al., 2009	12		26	960	II, n = 2; III, n = 5; IV, n = 5			2 (16.7)	3 (25.0)		7/19 (36.8)
Bassan et al., 2012	32	15:17			III, n = 15; IV, n = 17		2 (6.3)	0 (0)			

NA = not available.

including factors such as birth weight, gestational age at birth, and severity of IVH. Definitions of outcomes were not standardized among studies and so probably differed as well. Length of follow-up and statistical methods also varied among studies. Moreover, it is well recognized that there exist wide variations in practice patterns among different institutions⁵⁶ (including differing thresholds for surgical intervention and ancillary methods of medical management). Such variation almost certainly existed among the wide geographic and temporal range of our primary studies.

Such clinical heterogeneity, although almost certainly present in our primary studies, is very difficult to identify from published data. Statistical heterogeneity, however, is more objectively defined and easier to identify. We did find, for example, that statistical heterogeneity was generally low for the outcomes of infection, obstruction, arrest of hydrocephalus, and revision. That is, the outcomes reported were relatively consistent among studies. By contrast, there was substantial statistical heterogeneity among reported mortality rates and neurodevelopmental outcomes. This precluded us from being able to make meaningful comparisons between groups with respect to these latter outcomes.

This is perhaps not surprising. Certainly, IVH and PHVD/PHH are known to present with a very wide spectrum of clinical severity, so outcomes can be expected to vary between cohorts.^{49,52} These outcomes, in particular, are influenced to a great extent by a number of factors, e.g., gestational age, birth weight, grade of IVH, and the presence of other complications of prematurity. In addition, neurodevelopmental outcome is hard to quantify, and definitions of good neurodevelopmental outcome varied widely among included articles. For example, some studies relied on motor outcome, whereas others evaluated intellect, and still others used language. Because of all of these limitations, the present study represents only a current snapshot of the existing literature and cannot replace high-quality comparative studies, of which very few currently exist.

The 2 most common methods used to temporarily treat PHVD are VSGS and VAD, and there has appropriately been much interest in this comparison. One practical advantage that VSGSs offer over VADs is the ability to divert CSF to an anatomical compartment where it is directly reabsorbed into the body, thus circumventing the need for external CSF removal (i.e., serial tapping). In theory, this reduces the risk of infection. On the other hand, the maintenance of a closed system prevents the removal and allows the buildup of blood products and debris that may block the system, possibly increasing risk of mechanical failure. We found a slightly lower rate of infection (9.2% vs 9.5%) and higher rate of obstruction (9.6% vs 7.3%) with VSGSs compared with VADs. However, the 95% CIs overlapped, suggesting no statistically significant difference.

In 2009, Wellons and colleagues⁶⁶ published the results of a multicenter retrospective series examining conversion from temporary to permanent CSF diversion in infants with PHVD/PHH. This group observed a statistically significant difference in permanent shunt rate for premature infants temporized with VAD (61 of 88 patients [69%]) versus

FIG. 4. Forest plots of meta-analyses of outcomes and complications of EVD for treatment of PHVD in preterm infants. Obstruction (A); infection (B); arrest of hydrocephalus (C); death (D); good neurodevelopmental outcome (E); and revision (F).

VSGS (31 of 36 patients [86%]). A theoretical advantage often described for VSGS is the so-called back-pressure provided by the subgaleal space; this is believed to provide a driving force to kick-start the CSF absorptive pathways.

However, blood and debris are hypothesized to activate an inflammatory process mediated by various cytokines, such as tumor necrosis factor (TNF)- α and transforming growth factor (TGF)- β ; these stimulate the deposition of

extracellular matrix proteins, which ultimately obstruct CSF pathways.^{35,58,59,68}

The elimination of such cytokines by serial tapping may contribute to a lower shunt rate with use of VADs. On the other hand, CSF is thought to contain neurotrophic factors and molecules involved in nervous system signaling.^{43,65} Hence, CSF removal may have important implications for CNS development and function. In our study, we found VADs resulted in only a very slightly higher incidence of arrest of hydrocephalus that was not statistically significant (17.5% vs 13.9%). Neurodevelopmental outcomes were comparable for VADs and VSGSs after accounting for heterogeneity.

An important alternative to VADs and VSGSs are EVDs, which are used in many different settings to temporarily treat hydrocephalus, perhaps the most notable being subarachnoid hemorrhage.²¹ As with VSGSs, EVDs allow continuous drainage of CSF, without requiring repeated taps. However, like VADs, these devices also allow blood, debris, and inflammatory cytokines to be removed from the ventricular space to the external environment. We observed slightly lower rates of obstruction (6.8%) and infection (6.7%) for patients treated with EVDs compared with VADs and VSGSs, but again, these were not statistically significant. Although the external hardware of an EVD theoretically provides a route of entry into the CNS for microbes, the rates of infection and obstruction may have been lower because EVDs are often routinely replaced as a precautionary measure.

Indeed, as expected, the revision rate of EVDs (47.3%) was significantly greater than that of VADs (10.8%) or VSGSs (12.2%). However, it was not possible to discern from the information presented in individual articles what proportion of these revisions was elective versus secondary to failure. Furthermore, the rates of infection and obstruction reported in our study are consistent with those reported for EVDs in various other contexts.^{18,29,47,61} Interestingly, the rate of arrest of PHVD was substantially higher for treatment with EVD (31.8%) versus VAD (17.5%) or VSGS (13.9%). For the comparison between EVD and VSGS, this difference reached statistical significance, as indicated by the nonoverlapping CIs.

One hypothesis for this unexpected finding is that all EVDs require eventual removal, forcing a decision to either convert to a permanent shunt, or to stop CSF diversion altogether. The latter may result in a more thorough trial of the natural primary and secondary CSF pathways and a final opportunity to avoid permanent shunting in the infant. Given the numerous confounding factors and heterogeneity that we could not control for, it was not possible to fully attribute this difference to the use of EVDs alone. However, it is worthy of further investigation.

Importantly, our study does not, and cannot, replace the need for well-designed prospective comparative studies addressing these questions. Key components of a robust study on this topic would include randomization; stratification of patients by relevant prognostic factors, e.g., gestational age, grade of IVH, and presence/absence of other complications of prematurity; and multi-institutional design to generate sufficient power. Given the results presented here, we recommend direct comparison of EVD

in addition to VSGS and VAD for treatment of PHVD in preterm infants.

Conclusions

Our study provides a useful summary of the current literature on outcomes related to the use of VSGSs, VADs, and EVDs in the treatment of prematurity-related PVHD/PHH. The results of prospective comparative studies in this area will provide further, much-needed insights.

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Disclosure

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

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Conception and design: Kulkarni, Badhiwala, CJ Hong. Acquisition of data: Kulkarni, Badhiwala, CJ Hong, BY Hong, Riva-Cambrin. Analysis and interpretation of data: all authors. Drafting the article: Badhiwala, CJ Hong, Nassiri. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Kulkarni. Statistical analysis: Badhiwala, Nassiri. Administrative/technical/material support: Kulkarni, Riva-Cambrin. Study supervision: Kulkarni, Riva-Cambrin.

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