Childs Nerv Syst (2016) 32:1039–1048
DOI 10.1007/s00381-016-3095-1

ORIGINAL PAPER

International Infant Hydrocephalus Study: initial results of a prospective, multicenter comparison of endoscopic third ventriculostomy (ETV) and shunt for infant hydrocephalus

Abhaya V. Kulkarni[1] · **Spyros Sgouros**[2] · **Shlomi Constantini**[3] · **IIHS Investigators**

Received: 6 March 2016 / Accepted: 12 March 2016 / Published online: 23 April 2016

Abstract
Introduction The IIHS is an international, prospective, multicenter study to compare endoscopic third ventriculostomy (ETV) and shunt in infants (<24 months old) with symptomatic triventricular hydrocephalus from aqueductal stensosis. Recruitment started in 2004, and here, we present the first results of IIHS.
Methods IIHS utilized a prospective comprehensive cohort design, which contained both a randomized and a non-randomized arm. Patients received either an ETV or shunt, based on randomization or parental preference. Patients were followed prospectively for time to treatment failure, defined as the need for repeat CSF diversion procedure (shunt or ETV) or death due to hydrocephalus. Survival analysis was used to compare time to failure for ETV versus shunt. The trial was registered at clinicaltrials.gov (NCT00652470).
Results A total of 158 patients met eligibility criteria (median age at surgery 3.6 months, IQR 1.6–6.6 months) across 27 centers in 4 continents. Since only 52 patients (32.9 %) were randomized, all 158 patients were analyzed together (115 ETV, 43 shunt). Actuarial success rates for ETV vs shunt at 3, 6, and 12 months were as follows: 68 vs 95 %, 66 vs 88 %, and 66 vs 83 %. The 6-month ETV success rate of 66 % was slightly higher than would have been predicted by the ETV Success Score (57 %).The hazard ratio for time to treatment failure favored shunt over ETV (3.17, 95 % CI 1.45–6.96, p = 0.004), after adjusting for age at surgery, history of previous hemorrhage or infection, continent, and randomization status. Patients younger than 6 months of age appeared to do relatively worse with ETV than older patients.
Conclusions The IIHS has provided the first prospective direct comparison of ETV and shunt for infant hydrocephalus. These initial results suggest that shunting has a superior success rate compared to ETV, although the success rate for both was relatively high. This patient cohort continues to be followed, and we will await the results of the important primary outcome of health status at 5 years of age.

Keywords Endoscopic third ventriculostomy · Triventricular hydrocephalus · ETV Success Score

See "Appendix" for full list of study investigators

✉ Shlomi Constantini
Sconsts@netvision.net.il

[1] The Hospital for Sick Children, University of Toronto, 555 University Avenue, Suite 1503, Toronto, Ontario M5G 1X8, Canada

[2] Department of Pediatric Neurosurgery, Mitera Children's Hospital, University of Athens Medical School, Athens, Greece

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

Introduction

The optimal treatment for infant hydrocephalus is yet to be definitively determined [1–8]. Two main surgical options exist: endoscopic third ventriculostomy (ETV) and CSF shunt. Direct comparisons of the outcome of ETV and shunt are very few and limited, almost exclusively, to retrospective studies [9–13]. Based on the current, albeit limited, literature, a few conclusions can be drawn. Young age, especially under 1 year, is known to be a prognostic factor for ETV failure, but is likely also a

prognostic factor for shunt failure [13]. From a patient and family perspective, failure of either procedure requires repeat surgery and is, perhaps, equally detrimental, although, in the long-term, parental worry about complications seems to be less after ETV [14, 15]. Neither treatment appears to show a clearly superior long-term health-related quality of life outcome [10, 16–19]. Therefore, the debate regarding ETV versus shunt remains unresolved.

To help provide clarity, the International Infant Hydrocephalus Study (IIHS) was started in 2004, under the aegis of the International Federation of Neuroendoscopy (previously known as the International Study Group for Neuroendoscopy) [20]. The IIHS is an international, prospective, multicenter study that aimed to answer the question: in infants (<24 months old) with symptomatic triventricular hydrocephalus from aqueductal stenosis, does initial treatment with ETV result in superior or no worse outcome at 5 years of age compared to shunt? The primary outcome was the Health Utilities Index Score [17, 21] at 5 years of age. The population of infants (<24 months) with aqueductal stenosis is a unique group. Their young age makes them less-than-ideal candidates for ETV, but their etiology (pure obstructive hydrocephalus) is among the most favorable for ETV [22]. They are, therefore, an ideal population in which to compare ETV and shunt, since community equipoise appears to exist.

Recruitment for the IIHS ended in December 2013, and herein, we present the first set of analyses relating to treatment failure. The accrual of the 5-year outcome, which is the overall primary outcome of the IIHS, is continuing and that analyses will be presented in a future publication.

Methods

The IIHS was designed as a prospective comprehensive cohort study, which contained both a randomized and non-randomized arm [20, 23] See Appendix for further details regarding IIHS structure and personnel. Participating neurosurgical centers were all experienced in pediatric neuroendoscopy (≥10 neuroendoscopic procedures per year per surgeon and ≥2 ETV operations in infants per surgeon in total). Patients who met the following criteria were considered eligible for the study: <24 months of age at time of operation; symptomatic triventricular hydrocephalus (TVH) requiring first treatment; born at >36 weeks gestation; preoperative MRI showing aqueductal stenosis with no other major brain anomalies. Patients with a history of intraventricular hemorrhage (intrauterine or post-natal) or intracranial infection were included, unless this related to prematurity. Patients were excluded if they had the following: open spina bifida; Dandy Walker syndrome with vermian agenesis/dysgenesis; perinatal asphyxia; severe brain dysmorphic anatomical features; known chromosomal abnormality; or intracranial tumor. Eligibility criteria were independently adjudicated for all patients.

Intervention Patients were allocated to intervention using a comprehensive cohort design. The primary mode of treatment allocation was randomization. If families consented to randomization, the intervention was determined by 1:1 randomization, stratified by center. If families did not consent to randomization, they were enrolled in the treatment arm of their choice. The ETV intervention consisted of a standard frontal burr hole and use of an endoscopic camera to visualize the floor of the third ventricle. A ventriculostomy was created using the surgeon's own preferred method of perforation. At the surgeon's discretion, a post-operative temporary external ventricular drain or reservoir was inserted. The ventriculoperitoneal shunt intervention involved creating a burr hole in the frontal or occipital regions and cannulating the ventricle with a silastic catheter. This was then attached to a valve mechanism of the surgeon's choice and distal silastic tubing which ran subcutaneously to the peritoneal cavity. Prophylactic antibiotics were used.

Follow-up Following the initial intervention (ETV or shunt), patients were regularly followed as per departmental and surgeon's routine, but with scheduled visits at 1, 2, 3, and 5 years after surgery. Adverse events were documented. All data were collected prospectively. At enrolment, baseline clinical data were collected. Post-operative data were collected, including assessments of complications and treatment failures. As part of IIHS, patients underwent neurocognitive and imaging studies, but these data are still being collected and are not presented in this paper.

Treatment failure was defined as the need for any repeat intervention for definitive CSF diversion (including repeat ETV or shunt insertion/revision), as determined by the treating surgeon, following standard clinical practice, or death related to hydrocephalus. At treatment failure, the treating surgeon decided whether to repeat the original treatment (i.e., a repeat ETV for a patient in the ETV group or a shunt revision for a patient in the shunt group), or whether to "cross-over" (i.e., attempt an ETV for a shunted patient or insert a shunt for an ETV patient).

Sample size The study was initially expected to enroll 182 randomized patients and was powered to detect a 0.10 difference in 5-year health status using the Health Utilities Index [17]. Study recruitment began as early as 2005 in some centers, with staggered entry of new participating centers thereafter. However, enrolment in the randomized arm was slower than anticipated. Therefore, recruitment was stopped in December 2013, at the recommendation of the Data Safety Monitoring Committee (DSMC) on the basis of futility of reaching the targeted randomized cohort sample size. The DSMC suggested that analysis be focused on treatment failure data, pooling together the randomized and non-randomized arms, while continuing to follow previously enrolled patients for their 5-year primary outcome. In this paper, we present the data on surgical treatment failure.

Analysis For these analyses, the randomized and non-randomized arms were pooled to compare those who underwent ETV versus shunt as their first surgical intervention. Baseline data between these two groups were compared to determine imbalances in preoperative characteristics, using chi-squared or Mann-Whitney, as appropriate. Survival curves were constructed using the Kaplan-Meier method for time-to-first treatment failure and compared using log-rank test. The primary analysis of this paper was performed using Cox proportional hazards regression to compare time-to-first treatment failure of ETV versus shunt, adjusting for patient age (months), history of infection/hemorrhage (yes/no), geographical continent (since there were too few patients in each center to adjust by individual center), and randomization status (i.e., whether the patient entered the study in the randomized or non-randomized arm). Geographical continent was categorized as the Americas (since there only a few patients from North America alone), Europe, and Asia. Preoperative head circumference, analyzed as an age-corrected *Z* score, was not associated with treatment failure and, therefore, was not included for further analysis. Proportional hazards assumption was checked by assessing the significance of each variable as an interaction with time. Randomization status did not meet the proportional hazards assumption. Therefore, analysis was stratified by randomization status. Proportional hazards assumption was confirmed for all other variables.

The ETV Success Score (ETVSS) was calculated for each patient. The ETVSS provides the predicted chance of ETV success at 6 months (ranging from 0 to 90 %), based primarily on patient age and etiology of hydrocephalus [22]. We compared the ETVSS (predicted chance of ETV success) to the observed 6-month ETV success rate in our cohort.

The IIHS was publically registered (NCT00652470) and received ethics approval from all participating institutions. Participating investigators and other trial personnel are listed in the "Appendix" section.

Results

A total of 182 patients were initially enrolled in the study (Fig. 1). However, of these, 24 were eliminated after independent adjudication and were removed from further analyses (11 did not meet eligibility criteria, and 13 were missing important preoperative data). This left 158 patients from 27 centers in 4 continents (64 from Europe, 61 from Asia, 22 from South America, and 11 from North America), of whom 115 had ETV as first intervention (33 randomized, 82 non-randomized) and 43 had shunt as first intervention (19 randomized, 24

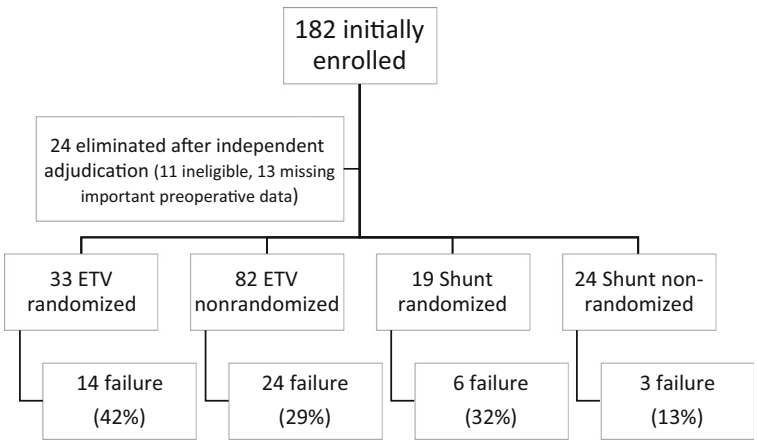

Fig. 1 Diagram showing the flow of patients through the study and their outcome results

Table 1 Patient characteristics

	Overall	ETV (n = 115)	Shunt (n = 43)	P value
Age in months (median, IQR)	3.6 (1.6–6.6)	4.3 (1.8–7.7)	2.2 (0.6–5.3)	0.007
Age categories (number, percent)				0.01
<30 days	29 (18.4 %)	15 (13.0 %)	14 (32.6 %)	
30 days to <6 months	83 (52.5 %)	60 (52.2 %)	23 (53.5 %)	
6 to <12 months	28 (17.7 %)	24 (20.9 %)	4 (9.3 %)	
12 to <24 months	18 (11.4 %)	16 (13.9 %)	2 (4.7 %)	
History of infection (number, percent)	9 (5.7 %)	4 (3.5 %)	5 (11.6 %)	0.06
History of hemorrhage (number, percent)	9 (5.7 %)	8 (7.0 %)	1 (2.3 %)	0.44
Randomized arm (number, percent)	52 (32.9 %)	33 (28.7 %)	19 (44.2 %)	0.09
Length of initial hospitalization, days (median, IQR)	5 (4–10)	5 (4–10)	5 (4–9)	0.76
Length of follow-up, days (median, IQR)	739 (69–1553)	738 (34–1536)	884 (268–1683)	0.15
Treatment failure (number, percent)	47 (29.7 %)	38 (33.0 %)	9 (20.9 %)	0.17

non-randomized). Baseline data for these patients are shown in Table 1. Baseline differences between the two were noted only for age, with shunt patients being younger at surgery.

Peri-operative complications included the following: 1 early CSF infection in the shunt group (2.3 %), 7 CSF leaks in the ETV group (6.1 %), and 1 perioperative seizure in the ETV group (0.9 %). There was no perioperative mortality. Overall shunt infection rate was 4.7 % (2 infections).

Median length of available follow-up was 739 days (IQR 69–1553), during which time, 38 ETV patients and 9 shunt patients demonstrated treatment failure. Among these failures, there was 1 hydrocephalus-related death (in the non-randomized shunt arm) due to presumed shunt failure in a child who died before being able to be transferred to the treating neurosurgical center. There were 3 other mortalities, but these were deemed to be not related to hydrocephalus after independent review and were not counted as treatment failures.

Table 2 shows the Kaplan-Meier estimates of ETV and shunt success at various time points. The ETV success was 66.3 % at 6 months and 64.1 % at 36 months, which was relatively stable. The shunt success was 87.8 % at 6 months and 79.1 % at 36 months.

Table 2 Kaplan-Meier estimates of treatment success

Time point after treatment (months)	ETV (n = 115) (%)	Shunt (n = 43) (%)
1	82.3	100
3	68.1	95.1
6	66.3	87.8
12	66.3	82.5
24	64.1	79.1
36	64.1	79.1

Unadjusted survival curves comparing time-to-first treatment failure for ETV and shunt are shown in Fig. 2. There was no significant difference in these curves (p = 0.07, log-rank). However, after adjusting for age, continent, history of infection/hemorrhage, and stratifying by randomization status, the adjusted hazard ratio for ETV was 3.17 (95 % confidence interval 1.45–6.96, p = 0.004), suggesting a significantly higher risk of treatment failure compared to shunt. Full results of the Cox regression are shown in Table 3. This model revealed that younger age was also associated with a greater chance of treatment failure (hazard ratio 0.89 (0.82–0.98), p = 0.015), regardless of type of treatment. Addition of an interaction term between type of treatment and age was not significant (p = 0.94). Continent and history of previous infection/hemorrhage were not significantly associated with treatment failure. The results were similar within both the randomized patient sample and the non-randomized patient sample.

In order to further investigate the association between age and treatment effect, separate survival curves were constructed for patients <6 months of age (N = 75 ETV and 37 shunt, Fig. 3a) and those ≥6 months (N = 40 ETV and 6 shunt, Fig. 3b). These revealed that the most dramatic relative difference in ETV versus shunt failure occurred in the <6-month-old group, where shunt was substantially better. However, the number of patients in the >6-month-group was very small, greatly limiting its interpretation.

The mean ETVSS, i.e., the predicted 6-month success rate, for the ETV patients was 57.0 %, which is slightly lower than the actual ETV 6-month success of 66.3 %.

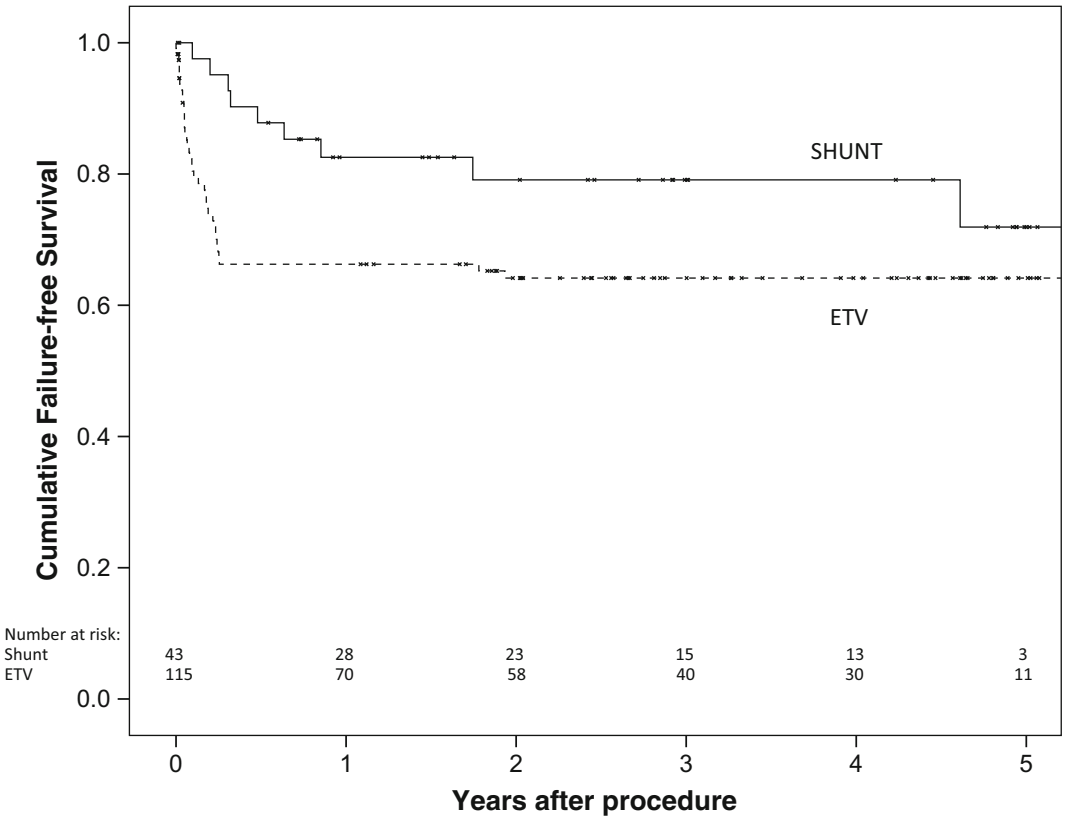

Fig. 2 Unadjusted Kaplan-Meier survival curves comparing time-to-first treatment failure for ETV and shunt for the entire cohort

For those operated at <6 months, the 6-month ETV success rate was 58.6 % (compared to an ETVSS of 48.0 %). For those ≥6 months, the 6-month ETV success rate was 79.5 % (compared to ETVSS of 74.0 %).

Discussion

We have presented the largest intervention study of infant aqueductal stenosis ever reported. Although modern ETV has been popular since the early 1990s, [24] the IIHS is the first ever multicenter, prospective comparison of ETV versus shunt in the literature. The participating centers, all experienced in neuroendoscopy, spanned 4 continents, which strengthens the external validity of our work. Data was collected prospectively, and importantly, we were able to adjust for baseline differences in age and history of infection or hemorrhage. The results of IIHS suggest that infants presenting with symptomatic triventricular hydrocephalus from aqueductal stenosis have higher rates of treatment failure with ETV compared to shunt. Despite this, the overall success rate of treatment was relatively high for both groups (64.1 % for ETV and 82.5 % for shunt at 1 year). In particular, the ETV group had a success rate at 6 months that was approximately 9 % higher than what would have been predicted by the ETV Success Score (66 versus 57 %). This difference was most obvious in the <6-month age group (actual success was 10.6 % higher than ETVSS) and less so in those >6 months old (actual success was only 5.5 % higher than ETVSS). This might be partially explained by the fact that the sample upon which the ETVSS was developed contained relatively few

Table 3 Results of Cox regression analysis for time-to-first treatment failure, stratified by randomization status

Variable	Hazard ratio (95 % confidence interval)	*P* value
ETV (compared to shunt)	3.17 (1.45–6.96)	0.004
Age (months)	0.89 (0.82–0.98)	0.015
History of infection/hemorrhage	1.49 (0.70–3.16)	0.31
Continent		0.70
Europe	Reference	
Asia	0.75 (0.38–1.48)	
North and South America	0.93 (0.43–2.02)	

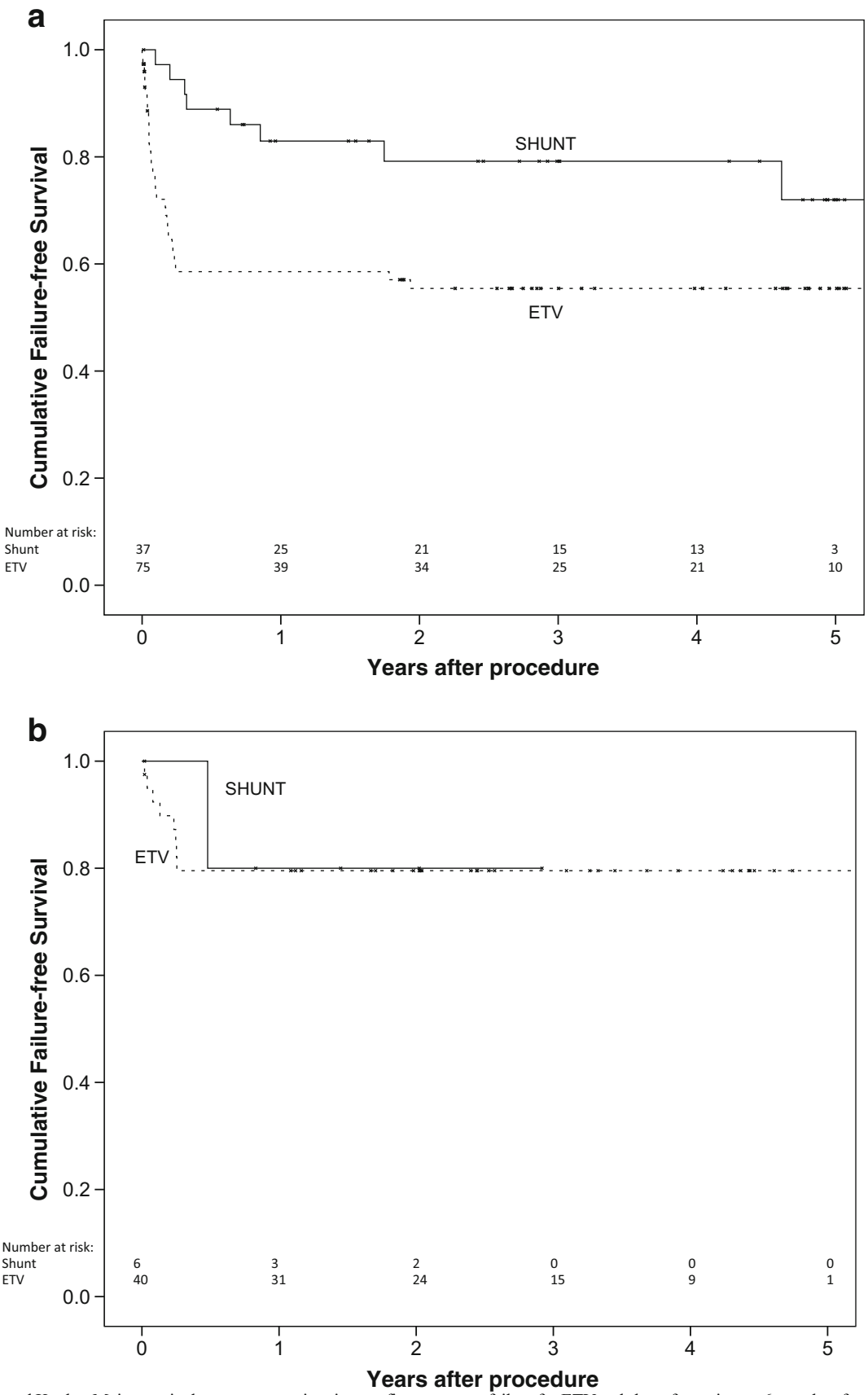

Fig. 3 Unadjusted Kaplan-Meier survival curves comparing time-to-first treatment failure for ETV and shunt for patients <6 months of age (Fig. 3a) and those ≥6 months (Fig. 3b)

infants (especially those <6 months old) with aqueductal stenosis, so its ability to predict accurately within such a sample is more limited [22]. The shunt group, as well, had notably lower rates of failure than both older [25] and more recent [26] prospective historical comparisons.

Neither procedure was associated with significant perioperative morbidity, although, notably, the rate of CSF leak in the ETV group was 6.1 %. A further finding in our study is that even within this infant group, younger age appeared to be associated with higher rate of treatment failure for both ETV and shunt. Although there was no significant statistical interaction between age and procedure performed, survival curves stratified by age (Fig. 3) showed that ETV appeared to have relatively higher failure compared to shunt for the youngest patients under 6 months of age. However, these curves, especially in the older age group, were limited by smaller sample size.

Our study has several limitations. Recruitment for our study ended prematurely, falling short of our intended sample size target. Regardless, this still represents the largest prospective study of its type, and the sample size was sufficient to show statistically significant differences. More worrisome, however, is that overall study enrollment was strongly biased towards ETV, with few patients in the randomized arm. This highlights the great difficulty in performing a randomized trial when comparing two such different surgical interventions, which often come with strong parental preferences. There was no independent adjudication of treatment failure in our study. There are, however, several features that serve to strengthen confidence in the validity of our data and, in particular, how treatment failure was determined. First, the observed temporal pattern of treatment failure of ETV and shunt was very similar to previous works [12, 27]. Second, the effect of age on treatment failure is also consistent with previous work [28–35]. Third, previous post hoc analyses have shown that independent adjudication in hydrocephalus trials have little impact on the final results compared to surgeon-determined treatment failure [36]. There were violations in study enrolment, with 24 patients needing to be removed after initial enrolment, following independent adjudication (Fig. 1). These patients were excluded from the final analysis, but resulted in an imbalance in the number of randomized patients in the ETV and shunt arm.

We did not include choroid plexus cauterization (CPC) with our ETV intervention. CPC, as an adjunct to ETV, has been suggested to improve the overall chances of ETV success, particularly in infants [37–39]. CPC was popularized only after our study began recruitment and currently is still not widely practiced in most settings [40, 41]. While our overall observed success with ETV was already quite high in this sample, it would be interesting to determine if there would be added beneficial effect from CPC. Further studies will need to compare the combined treatment of ETV with CPC against shunt, especially for the youngest infants and those with etiologies of hydrocephalus that are less favorable for ETV alone, such as intraventricular hemorrhage of prematurity or myelomeningocele.

In interpreting our results, it is important to note that the sample defined by our eligibility criteria is a relatively rare subset within the spectrum of pediatric hydrocephalus. Therefore, the applicability of our results to the wider hydrocephalus population remains to be determined. This group of infants with aqueductal stenosis was chosen because it was a relatively clean and homogenous population set that offered a focused controversial etiology with respect to treatment options, with community equipoise.

In summary, we interpret our results to suggest that, for at least this unique group of patients, initial treatment with ETV might be considered a reasonable alternative to shunt, with some important caveats. First, treatment failure was much higher in the youngest patients, especially under 6 months. In these patients, the use of ETV must be exercised with care, keeping in mind the greater risk of failure, which should be conveyed in discussions with families. This group is also one in whom the role of CPC might be beneficial and should be investigated. Second, the results presented in this analysis represent only a small part of the overall picture of outcome. Specifically, the overall primary outcome of the IIHS is health status at 5 years of age. Those important results, which are still pending, could alter the balance in favor of one treatment over the other.

Acknowledgments The authors would like to extend special thanks to Adina Sherer, who ran the organizational logistics of this study and without whom the IIHS would not have been possible.

Compliance with ethical standards

Conflict of interest The members of the Steering Committee have no conflicts of interest with respect to this work.

Appendix: IIHS personnel

Steering Committee: Shlomi Constantini (Principal Investigator), Spyros Sgouros, Abhaya V. Kulkarni

Consultant Neurologist: Yael Leitner

Data Safety Monitoring Committee: John RW Kestle (Chair), Douglas D Cochrane, Maurice Choux, Fleming Gjerris

Coordinating Administrator: Adina Sherer

Participating investigators (in parentheses are the number of eligible patients contributed to the study by each investigator)

Medical Center	IIHS participants	# of patients
Ankara, Turkey Hacettepe University Hospital	Nejat Akalan, Burçak Bilginer	(12)
Barcelona, Spain Hospital Sant Joan de Deu	Ramon Navarro (currently at Cleveland Clinic Abu Dhabi, UAE)	(7)
Belgrade, Serbia Clinical Center of Serbia, Belgrade, Neurosurgery Division	Ljiljana Vujotic	(8)
Berlin, Germany Charité—Universitätsmedizin Berlin	Hannes Haberl, Ulrich-Wilhelm Thomale	(4)
Birmingham, UK Birminghan Children's Hospital	Spyros Sgouros (currently at "Mitera" Childrens Hospital)	(1)
Buenos Aires, Argentina Hospital De Pediatria Prof. Dr. J.P. Garrahan	Graciela Zúccaro, Roberto Jaimovitch	(21)
Chicago, USA The University of Chicago Comer Children's Hospital	David Frim, Lori Loftis	(3)
Dallas, USA Children's Medical Center of Dallas	Dale M. Swift, Brian Robertson, Lynn Gargan	(6)
Debrecen, Hungary University of Debrecen, Clinical Center, Department of Neurosurgery	László Bognár, László Novák, Georgina Cseke	(5)
Genova, Italy Giannina Gaslini Hospital, Gaslini Children Institute	Armando Cama, Giuseppe Marcello Ravegnani	(3)
Giessen/Leipzig University Hospital Gießen and Marburg	Matthias Preuß Currently at University Hospital Leipzig	(4)
Greifswald, Germany Ernst-Moritz-Arndt-Universität Klinik für Neurochirurgie	Henry W. Schroeder, Michael Fritsch, Joerg Baldauf	(2)
Katowice, Poland Medical University of Silesia	Marek Mandera, Jerzy Luszawski, Patrycja Skorupka	(9)
Liverpool, UK Alder Hey Children's Hospital	Conor Mallucci, Dawn Williams	(4)
Lodz, Poland Polish Mother's Memorial Hospital, Research Institute	Krzysztof Zakrzewski, Emilia Nowoslawska	(2)
Lucknow (KGMC), India CSM Medical University (KGMC)	Chhitij Srivastava	(4)
Lucknow (SGPGI), India Sanjay Gandhi Postgraduate Institute of Medical Sciences (SGPGI)	Ashok K. Mahapatra, Raj Kumar, Rabi Narayan Sahu	(8)
Moscow, Russia Burdenko Neurosurgical Institute	Armen G. Melikian (Армен Меликян), Anton Korshunov (Антон Евгеньевич Коршунов), Anna Galstyan (Анна Галстян)	(11)
New Delhi, India All India Institute of Medical Sciences	Ashish Suri, Deepak Gupta	(12)
Nijmegen, The Netherlands Radboud University Medical Center	J. André Grotenhuis, Erik J. van Lindert	(9)
Nova Lima, Brazil Neurocirurgia Infantil, Biocor Instituto	José Aloysio da Costa Val	(5)
Rome, Italy Pediatric Neurosurgery, Policlinico Universitario "A. Gemelli"	Concezio Di Rocco, Gianpiero Tamburrini	(4)
São Paulo, Brazil Escola Paulista de Medicina, UNIFESP	Samuel Tau Zymberg, Sergio Cavalheiro	(3)
Shanghai, China Xinhua Hospital, Shanghai JiaoTong University School of Medicine	Ma Jie, Jiang Feng	(3)
Tel Aviv, Israel Dana Children's Hospital, Tel Aviv Medical Center	Shlomi Constantini, Orna Friedman	(20)
Toronto, Canada Hospital for Sick Children	Abhaya V. Kulkarni	(5)
Warsaw, Poland Children's Memorial Health Institute	Marcin Roszkowski, Slawomir Barszcz	(7)

The following centers (and investigators) participated in the IIHS, but did not enroll any patients: Baltimore, MD, USA (George Jallo); Gainesville, FL, USA (David W. Pincus, Bridget Richter); Kiel, Germany (HM Mehdorn, Susan Schultka); London, ON, Canada (Sandrine de Ribaupierre); London, UK (Dominic Thompson, Silvia Gatscher); Mainz, Germany (Wolfgang Wagner, Dorothee Koch); Reggio Calabria, Italy (Saverio Cipri, Claudio Zaccone); Winnipeg, MB, Canada (Patrick McDonald)

References

1. O'Brien DF, Seghedoni A, Collins DR, et al. (2006) Is there an indication for ETV in young infants in aetiologies other than isolated aqueduct stenosis? Childs Nerv Syst 22:1565–1572
2. Constantini S, Sgouros S, Kulkarni A (2013) Neuroendoscopy in the youngest age group. 79:S23
3. Fritsch MJ, Kienke S, Ankermann T, et al. (2005) Endoscopic third ventriculostomy in infants. J Neurosurg 103:50–53
4. Balthasar AJ, Kort H, Cornips EM, et al. (2007) Analysis of the success and failure of endoscopic third ventriculostomy in infants less than 1 year of age. Childs Nerv Syst 23:151–155
5. Wagner W, Koch D (2005) Mechanisms of failure after endoscopic third ventriculostomy in young infants. J Neurosurg 103:43–49
6. Gorayeb RP, Cavalheiro S, Zymberg ST (2004) Endoscopic third ventriculostomy in children younger than 1 year of age. J Neurosurg 100:427–429
7. Javadpour M, Mallucci C, Brodbelt A, et al. (2001) The impact of endoscopic third ventriculostomy on the management of newly diagnosed hydrocephalus in infants. Pediatr Neurosurg 35:131–135
8. Baldauf J, Oertel J, Gaab MR, Schroeder HWS (2007) Endoscopic third ventriculostomy in children younger than 2 years of age. Childs Nerv Syst 23:623–626. doi:10.1007/s00381-007-0335-4
9. Drake JM, Kulkarni AV, Kestle J (2009) Endoscopic third ventriculostomy versus ventriculoperitoneal shunt in pediatric patients: a decision analysis. Childs Nerv Syst 25:467–472. doi:10.1007/s00381-008-0761-y
10. Kulkarni AV, Hui S, Shams I, Donnelly R (2010) Quality of life in obstructive hydrocephalus: endoscopic third ventriculostomy compared to cerebrospinal fluid shunt. Childs Nerv Syst 26:75–79. doi:10.1007/s00381-009-0983-7
11. Rasul FT, Marcus HJ, Toma AK, et al. (2013) Is endoscopic third ventriculostomy superior to shunts in patients with non-communicating hydrocephalus? A systematic review and meta-analysis of the evidence. Acta Neurochir 155:883–889. doi:10.1007/s00701-013-1657-5
12. Kulkarni AV, Drake JM, Kestle JR, et al. (2010) Endoscopic third ventriculostomy vs cerebrospinal fluid shunt in the treatment of hydrocephalus in children: a propensity score-adjusted analysis. Neurosurgery 67:588–593. doi:10.1227/01.NEU.0000373199.79462.21
13. Kulkarni AV, Drake JM, Kestle JRW, et al. (2010) Predicting who will benefit from endoscopic third ventriculostomy compared with shunt insertion in childhood hydrocephalus using the ETV Success Score. J Neurosurg Pediatr 6:310–315. doi:10.3171/2010.8.PEDS103a
14. Kulkarni AV (2006) Questionnaire for assessing parents' concerns about their child with hydrocephalus. Dev Med Child Neurol 48:108–113
15. Kulkarni AV (2007) Assessment of mother and father concern in childhood hydrocephalus. Qual Life Res 16:1501–1509. doi:10.1007/s11136-007-9258-5
16. Kulkarni AV, Shams I (2007) Quality of life in children with hydrocephalus: results from the Hospital for Sick Children, Toronto. J Neurosurg 107:358–364. doi:10.3171/PED-07/11/358
17. Kulkarni AV, Cochrane DD, McNeely PD, Shams I (2008) Medical, social, and economic factors associated with health-related quality of life in Canadian children with hydrocephalus. J Pediatr 153:689–695. doi:10.1016/j.jpeds.2008.04.068
18. Kulkarni AV (2010) Quality of life in childhood hydrocephalus: a review. Childs Nerv Syst 26:737–743. doi:10.1007/s00381-010-1131-0
19. Kulkarni AV, Shams I, Cochrane DD, McNeely PD (2010) Quality of life after endoscopic third ventriculostomy and cerebrospinal fluid shunting: an adjusted multivariable analysis in a large cohort. J Neurosurg Pediatr 6:11–16. doi:10.3171/2010.3.PEDS09358
20. Sgouros S, Kulkharni AV, Constantini S (2006) The international infant hydrocephalus study: concept and rational. Childs Nerv Syst 22:338–345. doi:10.1007/s00381-005-1253-y
21. Feeny D, Furlong W, Boyle M, Torrance GW (1995) Multi-attribute health status classification systems. Health Util Index Pharmacoecon 7:490–502
22. Kulkarni AV, Drake JM, Mallucci CL, et al. (2009) Endoscopic third ventriculostomy in the treatment of childhood hydrocephalus. J Pediatr. doi:10.1016/j.jpeds.2009.02.048
23. Olschewski M, Schumacher M, Davis KB (1992) Analysis of randomized and nonrandomized patients in clinical trials using the comprehensive cohort follow-up study design. Control Clin Trials 13:226–239
24. Jones RF, Stening WA, Brydon M (1990) Endoscopic third ventriculostomy. Neurosurgery 26:82–86
25. Drake JM, Kestle JR, Milner R, et al. (1998) Randomized trial of cerebrospinal fluid shunt valve design in pediatric hydrocephalus. Neurosurgery 43:294–295
26. Kulkarni AV, Riva-Cambrin J, Butler J, et al. (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. doi:10.3171/2013.7.PEDS12637
27. Kestle J, Drake J, Milner R, et al. (2000) Long-term follow-up data from the shunt design trial. Pediatr Neurosurg 33:230–236
28. Furlanetti LL, Santos MV, De Oliveira RS (2013) The success of endoscopic third ventriculostomy in children: analysis of prognostic factors. Pediatr Neurosurg 48:352–359. doi:10.1159/000353619
29. Kulkarni AV, Riva-Cambrin J, Browd SR (2011) Use of the ETV Success Score to explain the variation in reported endoscopic third ventriculostomy success rates among published case series of childhood hydrocephalus. J Neurosurg Pediatr 7:143–146. doi:10.3171/2010.11.PEDS10296
30. Naftel RP, Reed GT, Kulkarni AV, Wellons JC (2011) Evaluating the Children's Hospital of Alabama endoscopic third ventriculostomy experience using the Endoscopic Third Ventriculostomy Success Score: an external validation study. J Neurosurg Pediatr 8:494–501. doi:10.3171/2011.8.PEDS1145
31. Breimer GE, Sival DA, Brusse-Keizer MGJ, Hoving EW (2013) An external validation of the ETVSS for both short-term and long-term predictive adequacy in 104 pediatric patients. Childs Nerv Syst 29:1305–1311. doi:10.1007/s00381-013-2122-8
32. García LG, López BR, Botella GI, et al. (2012) Endoscopic third ventriculostomy success score (ETVSS) predicting success in a series of 50 pediatric patients. are the outcomes of our patients predictable? Childs Nerv Syst 28:1157–1162. doi:10.1007/s00381-012-1836-3
33. Durnford AJ, Kirkham FJ, Mathad N, Sparrow OC (2011) Endoscopic third ventriculostomy in the treatment of childhood hydrocephalus: validation of a success score that predicts

long-term outcome. J Neurosurg Pediatr 8:489–493. doi:10.3171/2011.8.PEDS1166
34. Vogel TW, Bahuleyan B, Robinson S, Cohen AR (2013) The role of endoscopic third ventriculostomy in the treatment of hydrocephalus. J Neurosurg Pediatr 12:54–61. doi:10.3171/2013.4.PEDS12481
35. Azimi P, Mohammadi HR (2014) Predicting endoscopic third ventriculostomy success in childhood hydrocephalus: an artificial neural network analysis. J Neurosurg Pediatr 13:426–432. doi:10.3171/2013.12.PEDS13423
36. Kestle J, Milner R, Drake D (1999) An assessment of observer bias in the shunt design trial. Pediatr Neurosurg 30:57–61
37. 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
38. 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. doi:10.3171/2012.4.PEDS1253
39. Stone SSD, Warf BC (2014) Combined endoscopic third ventriculostomy and choroid plexus cauterization as primary treatment for infant hydrocephalus: a prospective North American series. J Neurosurg Pediatr 14:439–446. doi:10.3171/2014.7.PEDS14152
40. Kulkarni AV, Riva-Cambrin J, Browd SR, et al. (2014) Endoscopic third ventriculostomy and choroid plexus cauterization in infants with hydrocephalus: a retrospective Hydrocephalus Clinical Research Network study. J Neurosurg Pediatr 14:224–229. doi:10.3171/2014.6.PEDS13492
41. Chamiraju P, Bhatia S, Sandberg DI, Ragheb J (2014) Endoscopic third ventriculostomy and choroid plexus cauterization in posthemorrhagic hydrocephalus of prematurity. J Neurosurg Pediatr 13:433–439. doi:10.3171/2013.12.PEDS13219