Original Paper

Pediatric Neurosurgery

Pediatr Neurosurg 2010;46:221–226
DOI: 10.1159/000319365

Received: February 15, 2010
Accepted after revision: July 13, 2010
Published online: November 4, 2010

Long-Term Outcome after Treatment of Hydrocephalus in Children

Tobias Appelgren[a] Sofia Zetterstrand[c] Jörgen Elfversson[a, b] Daniel Nilsson[a, b]

[a]Institute of Neuroscience and Physiology, Sahlgrenska Academy, University of Gothenburg, and [b]Department of Neurosurgery, Sahlgrenska University Hospital, Gothenburg, and [c]AstraZeneca R&D, Mölndal, Sweden

Key Words
Hydrocephalus · Ventriculoperitoneal shunt · Endoscopic third ventriculostomy · Complication · Shunt infection

Abstract
Aims: To provide long-term outcome data after treatment of hydrocephalus in children, and to identify risk factors for ventriculoperitoneal shunt (VPS) failure. ***Methods:*** Endoscopic third ventriculostomy (ETV) and VPS procedures in children between 2001 and 2005 were reviewed. Data collected prospectively included age at surgery, sex, aetiology of hydrocephalus, gestational age, emergency/planned surgery, duration of surgery, time of day, surgeon's experience and other concomitant surgery. The mean follow-up was 4.7 years (min. 2 years). The endpoint was a new surgery due to failure of treatment, and the time to failure was noted. Risk factors for VPS failure were analysed by univariate Cox proportional hazards regression. ***Results:*** Ninety-eight patients were included, 76 with a VPS, 22 with an ETV. Fifty-five percent of ETV and 58% of VPS failed. Significant risk factors ($p < 0.05$) for VPS failure were prematurity (HR: 2.05; 95% CI: 1.12–3.76), concomitant procedure (HR: 2.07; 95% CI: 1.04–4.12) and long duration of surgery (HR: 1.23; 95% CI: 1.06–1.44), while sex, surgeon's experience, shunt type, at what department the surgery was performed, whether the surgery was acute or elective, and time of day were not. ***Conclusion:*** Treatment failure occurred in >50% of patients after ETV and VPS. Prematurity and concomitant surgery were major risk factors for VPS failure.

Introduction

In spite of the introduction of endoscopic techniques and improved shunt hardware, treatment of hydrocephalus remains one of the greatest challenges in paediatric neurosurgery. In a meta-analysis of ventriculoperitoneal shunt (VPS) complications including more than 20,000 paediatric patients, the authors found that the frequency of shunt failure is the same today as 40 years ago [1]. What was also clear from this study was that only a few studies have reported the long-term outcome (>2 years) after VPS insertion and/or endoscopic third ventriculostomy (ETV). The reported failure rates for the two methods are similar, 41–58% for VPS [2–5] and 26–48% in ETV [2, 6, 7]. A long-term follow-up is particularly important as the age of paediatric patients receiving a shunt is often less than a year and treatment is usually lifelong. Therefore long-term follow-up data are necessary to give informed treatment recommendations and risk estimations to par-

KARGER

Fax +41 61 306 12 34
E-Mail karger@karger.ch
www.karger.com

1016–2291/10/0463–0221$26.00/0

Accessible online at:
www.karger.com/pne

Daniel Nilsson
Department of Neurosurgery, Sahlgrenska University Hospital
Blå stråket 7, 5 tr
SE–413 45 Gothenburg (Sweden)
Tel. +46 702 868 575, Fax +46 3141 6719, E-Mail daniel.nilsson@neuro.gu.se

ents with a hydrocephalic child. Identifying risk factors for failure of the treatment is important to select the preferred method of treatment (VPS or ETV) and to optimize the timing of surgery.

In this population-based study we report long-term outcome after treatment of hydrocephalus in south-western Sweden from 2001 to 2005. The aim was to provide data on long-term results after treatment of hydrocephalus in terms of treatment failure, to compare failure rates after ETV and VPS and to identify risk factors for shunt failure.

Materials and Methods

This study was approved by the local ethical board. The study was done at the Sahlgrenska University Hospital, Gothenburg, Sweden, where all patients with a neurosurgical problem from the south-western region of Sweden (population approx. 2.1 million) are referred to. Data were entered into the electronic patient chart prospectively at the time of surgery as a part of the compulsory perioperative documentation, a procedure in effect since January 2001. The electronic patient chart was initially searched broadly for a procedure code starting with AAA (diagnostic intracranial procedures) or AAF (intracranial shunt procedures) according to the Swedish version of the NOMESCO (Nordic Medico-Statistical Committee) Classification of Surgical Procedures version 1.9 [8]. Patients aged 0–18 years having had a primary ETV or VPS performed between 2001 and 2005 at the Department of Neurosurgery and the Department of Paediatric Surgery (where most children <2 years of age are treated) at the Sahlgrenska University Hospital, Gothenburg, were selected for further analysis. Patient data including age at surgery, prematurity, sex, aetiology of hydrocephalus (categorized as tumour, intraventricular haemorrhage, infection, cyst, aqueductal stenosis, myelomeningocele, other malformation and other) and death during the study time were collected. Surgical data included procedure type (ETV or VPS), duration of surgery, emergency (defined as surgery within 24 h from clinical presentation of symptoms) or planned surgery, time of start of surgery, surgeon's experience (categorized as >20 or ≤20 procedures during the study time), whether surgery was performed at the Department of Neurosurgery or at the Department of Paediatric Surgery, and whether a concomitant surgical procedure was performed. For the analysis, all patient identification data were coded.

The endpoint was a failure of the first surgical treatment, requiring new surgery. The time to failure was noted as well as the type of failure (infection, mechanical failure of the shunt or non-functioning ETV). The diagnosis of a non-functioning ETV was made according to clinical criteria in patients with signs of increased intracranial pressure or growing head circumference and increase in ventricular size on imaging (usually CT). All surgical procedures were performed by a specialist in neurosurgery or a final-year resident. The severity of the treatment failures was categorized as minor (resolved within days without residual symptoms), medium (resolved within 3 months without residual symptoms), serious (persistent effect with mild sequelae) or catastrophic (persistent effect with serious sequelae or death). If there was no treatment failure, the patients were followed until May 1, 2008, for a minimum of 2 years and 4 months (mean: 4.7 years; range: 2.3–8 years).

All data are presented using descriptive statistics. Microsoft Excel was used for computations. Time to VPS failure was analysed in a Cox proportional hazards regression model (SAS version 8.2 was used for computations). Separate models were fitted for each available potential risk factor, and the relative risk for each risk factor was estimated in terms of the hazard ratio (HR) with the 95% CI and p value. $p < 0.05$ was considered significant.

Results

Ninety-eight patients were included, 76 had a VPS and 22 had an ETV (fig. 1). Ten children (45%) had a functioning ETV at follow-up (mean age: 7.8 years), and in 12 children (55%) the ETV failed during the follow-up period (mean age: 1.9 years). All ETV in children younger than 6 months (n = 9) failed during follow-up. ETV failure occurred after a mean time of 282 days (range: 10–1,348 days). Fifty-eight percent of VPS failed, 41% due to shunt obstruction and 17% due to infection. The mean time between VPS insertion and revision was 567 days (range: 10–2,453 days) for obstruction and 76.8 days (range: 3–572 days) for shunt infection. The Kaplan-Meier survival plots for VPS and ETV are shown in figure 2. Shunt obstruction was localized in the ventricular catheter in 19 patients (61%), in the shunt valve in 3 patients (10%), in the distal catheter in 6 patients (19%), and in 3 patients (10%), the site of obstruction was not reported.

The most common aetiologies were intraventricular haemorrhage for VPS and tumour for ETV (fig. 3). Most surgeries were planned, only 2 (9%) of the ETV patients and 7 (9%) of the VPS patients had an emergency procedure. Most procedures were single procedures, but in 7 (32%) of the ETV and 14 (19%) of the VPS cases, another, concomitant procedure was performed. These procedures were as follows: in the ETV group there were 3 tumour resections/biopsies, 2 cyst fenestrations and 1 external ventricular drainage, and in the VPS group there were 6 myelomeningocele closures, ventriculoscopy in 5 cases, tumour biopsy in 2 cases, and withdrawal of subcutaneous drainage in 1 case. The duration of the surgical procedures is shown in figure 4. Most surgeries were performed by 1 surgeon who was considered the reference surgeon for the statistical analysis. Shunt types used were Strata in 42 cases (55%), Delta in 32 cases (42%) – both from Medtronic (Medtronic Neurosurgery, Goleta, Calif., USA) – and Codman Medos (Codman, Raynham, Mass., USA) in 2 (3%) of the patients.

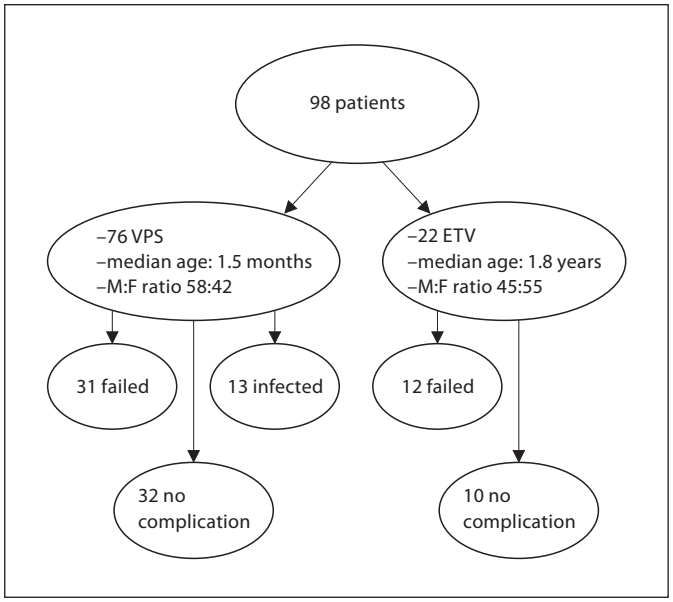

Fig. 1. Overview of included patients and outcome.

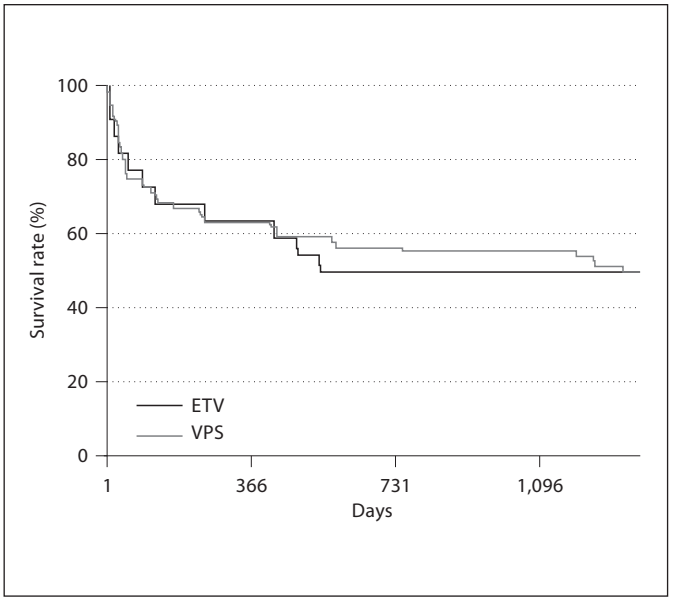

Fig. 2. Kaplan-Meier plot. Survival plots for VPS and ETV.

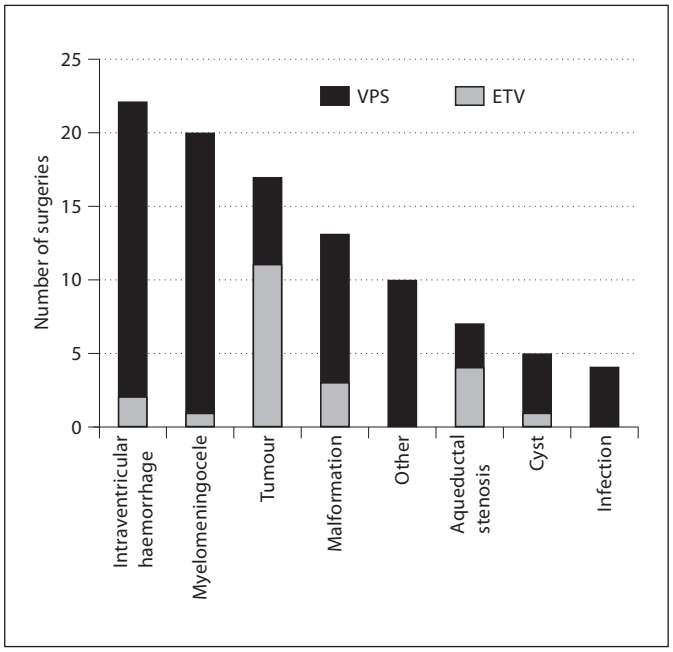

Fig. 3. Bar graph. Procedure frequency by aetiology.

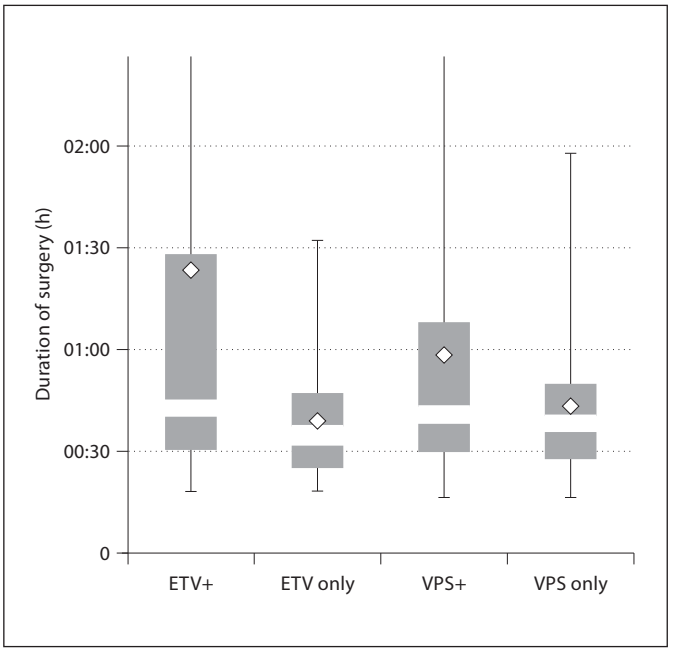

Fig. 4. Box-and-whisker plot. Duration of surgery for ETV and VPS as isolated procedures (ETV only and VPS only) and for all procedures, including procedures where another concomitant procedure was done (ETV+ and VPS+). For ETV+, maximum time was 9 h 18 min; for VPS+, maximum time was 4 h 43 min.

Table 1. Univariate Cox proportional hazards regression analysis for potential risk factors for VPS failure

	p	HR	95% CI for HR	
			lower limit	upper limit
Duration of operation (per 30-min increase)	0.0083	1.231	1.055	1.436
Premature (yes vs. no)	0.0195	2.054	1.123	3.757
Concomitant procedure (yes vs. no)	0.0392	2.066	1.037	4.116
Experience (>20 vs. ≤20 operations)	0.6282	0.863	0.476	1.566
Shunt type (Delta vs. Strata)	0.6641	1.150	0.612	2.160
Location (ND vs. PD)	0.7289	1.166	0.489	2.781
Emergency procedure (yes vs. no)	0.7326	1.163	0.488	2.772
Gender (female vs. male)	0.9326	0.974	0.533	1.780
Time of day (morning vs. afternoon)	0.9908	0.996	0.503	1.974

PD = Paediatric surgery department; ND = neurosurgical department.

Table 2. Results from 5 previous studies of shunt failure and from the present study

Study	Infection rate	Obstruction rate	Follow-up years	Number	Study type	Identified risk factors
Shah et al. [13]	–	27% (1 year)	1–5	7,399	retrospective multicentre	<2 months between revision (HR = 1.30); age of <30 days (HR = 2.02); aetiology (MMC, congenital higher); NE USA lower
McGirt et al. [4]	11%	42%	3.2	836	retrospective	low age; prematurity (HR = 2.15); IVH (HR = 2.62); number of shunts (HR = 1.31)
Kestle et al. [3]	8%	43%	1–3	344	prospective observational	–
Tuli et al. [5]	11%	44%	10	839	prospective observational	<6 months between revisions (HR = 1.72); prematurity (HR = 2.49); age: 40 weeks to 1 year (HR = 1.77); concurrent procedure (HR: 1.44–1.89)
Stein et al. [1]	–	49%	5	>10,000	meta-analysis	–
Current study	17%	41%	2.3–7	76	prospectively collected, retrospective analysis	prematurity (HR = 2.05); concomitant procedure (HR = 2.07); duration (HR = 1.007)

MMC = Myelomeningocele; NE = north-east; IVH = intraventricular haemorrhage.

In the Cox proportional hazards regression model, prematurity (HR = 2.05), concomitant procedure (HR = 2.07) and longer duration of operation (HR = 1.23) were found to be significant risk factors ($p < 0.05$) for failure of VPS, whereas surgeon's experience, shunt type (Strata or Delta), department, emergency/elective surgery, patient gender or time of day were not found to be significant risk factors (table 1). As the number of ETV was low (n = 22), further statistical analysis using Cox's proportional hazards regression model was not considered meaningful.

Discussion

In this long-term follow-up of treatment for hydrocephalus, 55% of ETV and 58% of VPS failed. The rate of ETV failure has been reported by Tuli et al. [7] to be 44% after a follow-up of 1–10 years in 32 patients. Similarly, Drake [6] reported a 5-year failure rate of 48% in 368 patients across Canada. In the study by de Ribeaupierre et al. [2], however, the 5-year failure rate after ETV was only 26%.

Patient selection criteria, geographical/regional conditions and patient referral patterns differ between cen-

tres, making studies on the treatment of hydrocephalus difficult to compare. One crucial factor to consider when comparing studies is the age of the treated patients as low age is well known to be an important risk factor both in ETV and VPS failure. In the present study, the median age of the ETV patients was 1.8 years, compared to 6 years in the Swiss study [2], 8.1 years in the study by Tuli et al. [7] and 4.8 years in the Canadian multicentre study [6]. This difference in the patient population can explain the higher failure rate after ETV in this study. Even though the population size in the ETV group did not permit further statistical analysis, we could see that the failure rate for ETV patients was higher in the paediatric surgery department, where the youngest children were treated. On the 'ETV success score' proposed by Kulkarni et al. [9], based on data from 618 ETV, low age (particularly below 6 months) was found to be the most important negative factor. This study, in which all ETV performed on children younger than 6 months ceased to function during follow-up, supports these findings.

Forty-one percent of the VPS patients developed a mechanical failure, compared to an obstruction rate of 42–49% in four previous, large studies [1, 3–5] (table 2). The majority of shunt failures were due to a blocked ventricular catheter, which has also been found by others. All ventricular catheters were placed frontally, which may reduce the risk of blockage of the holes of the ventricular catheter by choroid plexus or brain parenchyma compared to a parietal trajectory. Studies of shunt survival rate as a function of frontal or parietal trajectory have come to different conclusions on which should be the preferred location [10–12]. The only randomized study [11] found a slightly lower revision rate for a parietal catheter location; however, to resolve this issue, a larger randomized study would be needed.

Low age or prematurity have been found to be significant risk factors for shunt failure in previous studies, with HR in a narrow range of 2.02–2.49, compared to 2.05 in the present study (table 2) [4, 5, 13]. One previous study has found another concurrent procedure to be a risk factor with an HR of 1.77, similar to what we found (2.07), whereas McGirt et al. [14], analysing 820 VPS procedures, found use of the endoscope to be a risk factor for shunt infection (RR = 1.58) [5, 14]. Thus there is converging evidence that prematurity/low age, but possibly also a concurrent procedure, increase the risk of shunt failure. As a concurrent procedure prolongs the duration of surgery, the finding that long duration of surgery was found to be a risk factor for shunt failure (HR = 1.23 with every 30-min increase in time) may reflect this. Other risk factors previously studied include short time between revisions, aetiology of myelomeningocele and high number of previous shunts [5, 13]. As we only studied first-time shunts, we have no data on risk factors involving revisions, as for aetiology as a risk factor, our population was too small to allow any conclusions.

In this study, 17% of the patients developed a shunt infection. Shunt infection rates per patient in children vary widely in the literature, but they are 5–20% with a few exceptions [15]. In a recent study of 1,173 children with a median age of 4 months, 158 (13.6%) developed a shunt infection [16]. The authors found an age of <4 months to be a risk factor for shunt infection with an HR of 1.81. McGirt et al. [14] studied 442 patients with a mean age of 7.6 years, reporting an 11% infection rate and an increased risk of infection in premature patients, with an HR of 4.81. Similar infection rates were reported from a multicentre study of shunt valves, with 8.4% infections, the mean age of the children not being reported [3].

Thus the infection rates in the present study seem higher than in the studies mentioned above. The median age of shunted patients in this study was only 1.5 months, which is significantly lower than in similar studies, and 33 of 76 children (40%) were premature (<37 gestational weeks at birth). This may at least partly explain the high incidence of infection in this study, which is nonetheless worrisome, and mandates a close follow-up of infection rates. The low mean age and high proportion of preterm babies in our population may be a result of low infant mortality and good neonatal care in Sweden [17, 18]. This may lead to more preterm babies with severe neurological conditions (severe intraventricular haemorrhage, malformations, meningitis, etc.) surviving and needing treatment for hydrocephalus.

Several studies have reported reduced shunt infection rates after the introduction of shunt protocols. These usually include shunt surgery as first surgery of the day, minimizing the number of persons and traffic in the operating room, meticulous draping and wound closure and an experienced surgical team. Choux et al. [19] reported a spectacular reduction in infection rates from 15.6% before to 1% after the start of a new routine. Rotim et al. [20] reported 18% shunt infections in 201 children over 5 years, which fell to 8% following the implementation of a more rigorous shunt protocol. Decreased rates of shunt infections can be achieved also in premature patients, as has been shown by Pirotte et al. [15] reporting a <1% infection rate overall after applying a shunt protocol. Thus the revision of shunt protocols and monitoring of their application is an effective way of reducing shunt in-

fections. Antibiotic impregnation of ventricular catheters has been shown to reduce ventriculitis after external ventricular drainage in a randomized study; however, whether this is also true for shunts has not been systematically studied [21].

We recognize limitations of this study, including the small population size and the retrospective nature of the data review. However, the prospective data collection and use of unique nationwide social security numbers allowed us to retrieve data even if the patient had moved or was treated in another unit later. As our centre is the only referral centre in the region, all patients having a treatment failure were referred to our unit. This minimized missing data and patients lost to follow-up. In the statistical analysis, no correction for multiple comparisons was made, but the selection of risk factors was based on nominal p values, an appropriate approach given the exploratory nature of the study. The choice of the endpoint 'treatment failure requiring new surgical procedure' could be discussed. This approach was selected as it is simple to define and produces reliable data for further analysis.

Conclusion

Fifty-five percent of ETV and 58% of VPS failed in this long-term follow-up after treatment for hydrocephalus. Prematurity and concomitant surgery were identified as significant risk factors for VPS failure, with HRs of 2.05 and 2.07, respectively, whereas surgeon's experience, shunt type and emergency surgery were not linked to increased risk of VPS failure. Our study confirmed prematurity as a risk factor for shunt failure and suggests that shunting should be done as a single procedure, avoiding concurrent procedures which may significantly prolong the duration of surgery.

Acknowledgement

T.A. was supported by a grant from Stiftelsen Fru Mary von Sydows, född Wijk, donationsfond.

References

1 Stein SC, Guo W: Have we made progress in preventing shunt failure? A critical analysis. J Neurosurg Pediatr 2008;1:40–47.
2 de Ribaupierre S, Rilliet B, Vernet O, Regli L, Villemure JG: Third ventriculostomy vs ventriculoperitoneal shunt in pediatric obstructive hydrocephalus: results from a Swiss series and literature review. Childs Nerv Syst 2007;23:527–533.
3 Kestle J, Drake J, Milner R, Sainte-Rose C, Cinalli G, Boop F, Piatt J, Haines S, Schiff S, Cochrane D, Steinbok P, MacNeil N: Long-term follow-up data from the Shunt Design Trial. Pediatr Neurosurg 2000;33:230–236.
4 McGirt MJ, Leveque JC, Wellons JC 3rd, Villavicencio AT, Hopkins JS, Fuchs HE, George TM: Cerebrospinal fluid shunt survival and etiology of failures: a seven-year institutional experience. Pediatr Neurosurg 2002;36:248–255.
5 Tuli S, Drake J, Lawless J, Wigg M, Lamberti-Pasculli M: Risk factors for repeated cerebrospinal shunt failures in pediatric patients with hydrocephalus. J Neurosurg 2000;92:31–38.
6 Drake JM: Endoscopic third ventriculostomy in pediatric patients: the Canadian experience. Neurosurgery 2007;60:881–886, discussion 881–886.
7 Tuli S, Alshail E, Drake J: Third ventriculostomy versus cerebrospinal fluid shunt as a first procedure in pediatric hydrocephalus. Pediatr Neurosurg 1999;30:11–15.
8 Socialstyrelsen: Klassifikation av kirurgiska åtgärder 1997, ed 2. Stockholm, Swedish National Board of Health and Welfare, 2004.
9 Kulkarni AV, Drake JM, Mallucci CL, Sgouros S, Roth J, Constantini S: Endoscopic third ventriculostomy in the treatment of childhood hydrocephalus. J Pediatr 2009;155:254–259.e1.
10 Albright AL, Haines SJ, Taylor FH: Function of parietal and frontal shunts in childhood hydrocephalus. J Neurosurg 1988;69:883–886.
11 Bierbrauer KS, Storrs BB, McLone DG, Tomita T, Dauser R: A prospective, randomized study of shunt function and infections as a function of shunt placement. Pediatr Neurosurg 1990;16:287–291.
12 Dickerman RD, McConathy WJ, Morgan J, Stevens QE, Jolley JT, Schneider S, Mittler MA: Failure rate of frontal versus parietal approaches for proximal catheter placement in ventriculoperitoneal shunts: revisited. J Clin Neurosci 2005;12:781–783.
13 Shah SS, Hall M, Slonim AD, Hornig GW, Berry JG, Sharma V: A multicenter study of factors influencing cerebrospinal fluid shunt survival in infants and children. Neurosurgery 2008;62:1095–1102, discussion 1102–1103.
14 McGirt MJ, Zaas A, Fuchs HE, George TM, Kaye K, Sexton DJ: Risk factors for pediatric ventriculoperitoneal shunt infection and predictors of infectious pathogens. Clin Infect Dis 2003;36:858–862.
15 Pirotte BJ, Lubansu A, Bruneau M, Loqa C, van Cutsem N, Brotchi J: Sterile surgical technique for shunt placement reduces the shunt infection rate in children: preliminary analysis of a prospective protocol in 115 consecutive procedures. Childs Nerv Syst 2007;23:1251–1261.
16 Vinchon M, Dhellemes P: Cerebrospinal fluid shunt infection: Risk factors and long-term follow-up. Childs Nerv Syst 2006;22:692–697.
17 Gapminder. 2006. http://www.Gapminder.Org/data/.
18 CIA: The world fact book: country comparison. Infant mortality rate 2010. https://www.cia.gov/library/publications/the-world-factbook/rankorder/2091rank.html?countryName=Egypt&countryCode=EG&regionCode=af
19 Choux M, Genitori L, Lang D, Lena G: Shunt implantation: reducing the incidence of shunt infection. J Neurosurg 1992;77:875–880.
20 Rotim K, Miklic P, Paladino J, Melada A, Marcikic M, Scap M: Reducing the incidence of infection in pediatric cerebrospinal fluid shunt operations. Childs Nerv Syst 1997;13:584–587.
21 Zabramski JM, Whiting D, Darouiche RO, Horner TG, Olson J, Robertson C, Hamilton AJ: Efficacy of antimicrobial-impregnated external ventricular drain catheters: a prospective, randomized, controlled trial. J Neurosurg 2003;98:725–730.