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Original Article

Ventriculoperitoneal Shunt Outcomes among Infants

Hidehiko Maruyama*, Yusei Nakata, Akane Kanazawa, Hirokazu Watanabe,
Yusuke Shigemitsu, Yuka Iwasaki, Chiho Tokorodani, Mari Miyazawa,
Ritsuo Nishiuchi, and Kiyoshi Kikkawa

Department of Pediatrics, Kochi Health Sciences Center, Kochi 781-8555, Japan

Ventriculoperitoneal shunts (VPSs) are used for the treatment of hydrocephalus. Here we analyzed the outcomes of VPS placements in 24 infants to determine the risk factors for shunt failure. The infants had undergone the initial VPS operation in our hospital between March 2005 and December 2013. They were observed until the end of January 2014. We obtained Kaplan-Meier curves and performed a multivariate Cox regression analysis of shunt failure. Of the 24 cases, the median (range) values for gestational age, birth weight, and birth head circumference (HC) were 37 (27–39) wks, 2,736 (686–3,788) g, and 35.3 (23.0–45.3) cm, respectively. The total number of shunt procedures was 45. Shunt failure rates were 0.51/shunt and 0.0053/shunt/year. Shunt infection rates were 0.13/shunt and 0.0014/shunt/year. The Kaplan-Meier analysis revealed an increased risk for shunt failure in infants < 1 month old or in the HC > 90% tile. The Cox regression analysis yielded hazard ratios (HRs) of 2.93 (95% confidence interval (CI), 0.96–10.95, $p = 0.059$) for age < 1 month, and 4.46 (95% CI: 1.20–28.91, $p = 0.023$) for the HC > 90% tile. The multivariate Cox regression analysis showed adjusted HRs of 17.56 (95% CI: 2.69–202.8, $p = 0.001$) for age < 1 month, and 2.95 (95% CI: 0.52–24.84, $p = 0.228$) for the HC > 90% tile. Our findings thus revealed that the risk factors for shunt failure in infants include age < 1 month at the initial VPS placement.

Key words: head circumference, shunt failure, shunt infection, ventriculoperitoneal shunt

The use of ventriculoperitoneal shunts (VPSs) for the treatment of hydrocephalus poses the risk of shunt failure due to infection or obstruction. Shunt failure rates have been reported to range from 20% to 70% [1–4], with risk factors including young age, male, and socioeconomic status [5]. Shunt infection rates have been reported to range from 8% to 20% [6–13], with risk factors including prematurity [6, 8, 10], previous shunt infection [10, 12], postoperative cerebrospinal fluid (CSF) leaks [8], and young age [11–13]. Shunt failure, particularly

that due to infection, remains a significant problem in neurological surgery. This study assessed the outcomes of infantile VPS placement to determine the risk factors for shunt failure.

Patients and Methods

We conducted a retrospective cohort study in infants with VPSs who were admitted to the tertiary neonatal intensive care unit at Kochi Health Sciences Center between March 1, 2005 and December 31, 2013. The inclusion criteria required the infants to

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*Corresponding author. Phone: +81-88-837-3000; Fax: +81-88-837-6766
E-mail: maruyamahidehiko@gmail.com (H. Maruyama)

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have had an initial VPS placement at the study hospital within 1 yr after birth. Infants who had undergone an intracranial operation before their initial VPS placement were excluded. The study observation period continued through January 31, 2014.

Perinatal and neonatal data were collected at and after birth, including birth characteristics (sex, gestational age [GA], birth weight [BW], and head circumference [HC]), causes of hydrocephalus (aqueductal stenosis, brain tumor, CSF infection, head injury, intraventricular hemorrhage, myelomeningocele, or other/unknown), VPS-related factors at the time of placement (age, weight, HC, insertion site, operator, HC change after operation, and complications within 1 wk after the operation). After the initial VPS placement, the patients were monitored for shunt failure. Ventriculoatrial shunts were considered VPSs. Shunt failure rates and infection rates were calculated for all VPSs.

We generated Kaplan-Meier survival curves to estimate the risk of shunt failure. In addition, hazard ratios (HRs), corresponding 95% confidence intervals (95% CIs), and *p*-values were calculated using univariate and multivariate Cox regression analyses. The following risk factors were used in the multivariate Cox regression analysis: male [2], age < 1 month, HC > 90%tile at initial VPS placement, and occipital insertion [3]. Participating infants were divided by age at the time of the initial VPS placement, with age groups consisting of “< 1 month” and “≥ 1 month,” because younger age was considered to be a risk factor [5]. The additional risk factor of HC > 90%tile was also included. Although none of the previous studies reviewed had addressed this risk factor for shunt failure, macrocephaly is related to the severity of the disease. *P*-values < 0.05 were considered significant.

Shunt failure was defined as the need for any subsequent surgical procedure for definitive CSF diversion (due to shunt malfunction or infection), or death associated with hydrocephalus management [14]. A verified diagnosis of shunt infection required at least one of the following criteria: surgical wound infection or wound breakdown; positive CSF culture from shunt aspirate obtained using sterile procedures; bacteremia in patients with ventriculoatrial shunts; and peritoneal infection in patients with VPS [8]. The HC reduction rate was defined as follows:

$$\text{HC reduction rate} = \frac{(\text{HC at initial VPS placement} - \text{Minimum HC within 3 days after initial VPS placement})}{\text{HC at initial VPS placement}}$$

Statistical analyses were performed using JMP 10.0.2 software (SAS Institute, Cary, NC, USA). This study was approved by the Institutional Review Board of the Kochi Health Sciences Center.

Results

A total of 24 infants were evaluated in this study (Table 1), 13 (54%) of whom were male. The median (range) values for GA, BW, and birth HC were 37 wks + 4 days (27 wks + 1 day to 39 wks + 5 days, *n* = 23), 2,736 g (686 – 3,788 g, *n* = 23), and 35.3 cm (23.0 – 45.3 cm, *n* = 20), respectively. The causes of hydrocephalus were: myelomeningocele (*n* = 10), aqueductal stenosis (*n* = 6), interhemispheric cyst (*n* = 2), prematurity (*n* = 2), tumor (*n* = 1), Dandy-Walker syndrome (*n* = 1), and unknown (*n* = 2). The median (range) values for age, weight, and HC at the initial VPS placement were 0 month (0–11 months), 3.3 kg (2.2–10.2 kg), and 39.5 cm (33.5–49.4 cm, *n* = 22), respectively.

The number of participants < 1 month old was 15 (63%). The number of participants in the HC > 90%tile at the initial VPS placement was 15 (68.2%, *n* = 22). The number of occipital insertions of initial VPSs was 17 (71%). The major surgeon was A, who operated on 20 cases (83%). The complications that occurred within 1 wk after the initial VPS insertion were: CSF leakage (*n* = 7), including 1 case with fever, intracranial hemorrhage (*n* = 3), subdural hygroma (*n* = 1), and none (*n* = 14). For the three intracranial hemorrhage cases, the HC reduction ratios were 6.7% and 9.1% (the data of one case were missing). The mean (standard deviation [SD]) value of HC reduction in the infants without hemorrhage was 1.1% (3.1%) (*n* = 12).

The median (range) observation period following the initial VPS placement was 52 (1–99) months, with a total observation period of 1,147 months. Three cases were censored, including one infant who passed away due to causes unrelated to VPS, and 2 infants who were transferred.

The total number of VPSs was 45, with a shunt failure rate of 51.1%/shunt, or 0.53%/shunt/year.

Table 1 Characteristics of the 24 infants with VPS

Variable	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
Sex	F	F	M	M	M	F	M	M	F	M	M	M	M	F	F	F	M	M	F	F	F	M	F	M
Gestational age (week)	27	36	NA	34	38	38	38	37	30	38	38	36	37	34	37	37	38	37	38	39	37	37	39	37
Birth weight (g)	686	1,960	NA	2,110	2,970	2,810	3,280	2,605	1,621	3,220	3,312	2,812	2,736	1,800	2,178	2,528	3,788	2,218	2,990	3,322	3,488	2,498	2,674	3,262
Birth HC (cm)	23	29	NA	37	35.5	26.2	33.5	NA	28	34	39	35	38	35.5	NA	NA	45.3	30.5	40	34	43.5	41.5	33.5	43.3
Cause of hydrocephalus	Pre	AS	AS	MM	MM	MM	TU	AS	Pre	IC	UK	MM	AS	DW	MM	MM	AS	MM	MM	UK	IC	MM	MM	AS
Age (month)	11	5	7	0	0	0	0	9	2	1	0	0	0	1	0	5	0	0	0	4	0	0	0	0
Age (day)				0	0	0	11				5	0	7		0		7	20	0		8	0	20	13
Weight (kg)	6.8	6.3	10.2	2.2	3.0	2.8	3.3	6.6	3.3	5.5	3.3	2.8	2.7	2.6	2.2	7.9	3.8	2.7	3.0	8.3	3.3	2.5	3.4	3.3
HC (cm)	46.0	46.2	49.4	37.0	35.5	36.2	33.5	48.0	36.4	38.8	39.0	35.0	38.0	NA	NA	43.0	45.3	33.5	40.0	48.0	43.6	41.5	38.5	45.7
HC > 90%tile	-	+	+	+	+	+	-	+	-	-	+	-	+	NA	NA	-	+	-	+	+	+	+	+	+
Occipital insertion	-	-	-	-	-	-	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Initial VPS Surgeon	C	A	A	A	A	A	A	A	A	A	A	A	A	B	A	B	A	A	A	A	A	A	A	C
Place-ment	-	-	LE	-	-	-	-	-	LE	-	LE	-	LE	IH	SH	-	IH	-	-	LE	IH	LE	-	LE
HC reduction rate	-2.2	1.1	NA	8.1	NA	-0.6	NA	NA	NA	NA	0.8	-1.4	NA	NA	NA	NA	9.1	-0.6	3.5	-0.8	6.7	0	-0.5	5.9
SF	-	+	+	+	+	+	+	-	+	-	+	-	+	+	-	-	-	-	+	+	+	+	+	+
OP to SF (month)		50	22	20	18	0	8		60		49		41	4					0	1	1	1	0	1
Cause of SF within 6 months						Ob								Ob			li	Mi	Mi	Mi	Ob	Ob	In	In
Total OP (month)	6	99	91	97	92	90	89	80	77	77	71	11	59	41	55	49	27	18	8	3	6	4	2	1
Total VPS (VAS)	1	2	2	2	5(1)	3	3	1	2	1	2	1	4(1)	2	1	1	1	1	1	2	2	2	2	1

AS, aqueductal stenosis; CSF, cerebrospinal fluid; DW, Dandy-Walker syndrome; F, female; HC, head circumference; IC, interhemispheric cyst; IH, intracranial hemorrhage; li, insertion to inferior horn; In, infection; LE, CSF leakage; M, male; Mi, migration; MM, myelomeningocele; NA, not applicable; Ob, obstruction; OP, observation period; Pre, prematurity; SF, shunt failure; SH, shunt failure; TU, tumor; UK, unknown; VAS, ventriculoatrial shunt.

The shunt infection rate was 13.3%/shunt, or 0.14%/shunt/year. The number of shunt failures occurring within 6 months of initial VPS placement was eight. The causes of failure were: obstruction ($n=3$), infection ($n=2$), migration ($n=2$) (Fig. 1), and insertion to the inferior horn ($n=1$) (Fig. 2). The causative organisms in both infection cases were found to be coagulase-negative Staphylococci. One infection case and both migration cases had CSF leakage. No clear causes were identified for the shunt obstruction and the insertion to the inferior horn.

We performed a Kaplan-Meier analysis to evaluate the probability of failure-free survival (Fig. 3). Clear differences regarding age and HC at initial VPS placement were revealed by the analysis. There was an increased risk of VPS failure in both the infants < 1 month old compared to those ≥ 1 month old, and among the infants in the HC $> 90\%$ tile compared to those in the $\leq 90\%$ tile.

The Cox regression analysis yielded HR values of 2.93 (95% CI: 0.96–10.95, $p=0.059$) for age < 1 month and 4.46 (95% CI: 1.20–28.91, $p=0.023$) for the HC $> 90\%$ tile (Table 2). The survival curves for sex and insertion site crossed each other. The multivariate analysis showed adjusted HR values of 0.15 (95% CI: 0.03–0.57, $p=0.006$) for male sex, 17.56 (95% CI: 2.69–202.8, $p=0.001$) for age < 1 month, 2.95 (95% CI: 0.52–24.84, $p=0.228$) for the HC $> 90\%$ tile, and 0.64 (95% CI: 0.18–2.44, $p=0.494$) for occipital VPS insertion (Table 3). This result showed that the factors of sex and age made a significant difference, and that the HR for males was greatly decreased. There were 2 cases with missing data of HC at the initial VPS placement. We performed the sensitivity analysis by imputing tentative data: the adjusted HRs for male sex were from 0.19 to 0.46 ($p=0.010$ to 0.155).

Discussion

According to the results of our multivariate Cox regression analysis, the risk factors for shunt failure include female sex and age < 1 month at the initial VPS placement. A previous study found that patients < 1 month old had an increased risk of shunt failure [5]. This age factor would be related to poorly developed humoral and cellular immune systems, the immaturity of the skin barrier, and the feature of



Fig. 1 Shunt migration was found at the posterior head by X-ray in this 2-month-old female infant.



Fig. 2 The tip of the shunt was found in the inferior horn by head computed tomography in this 16-day-old male infant.

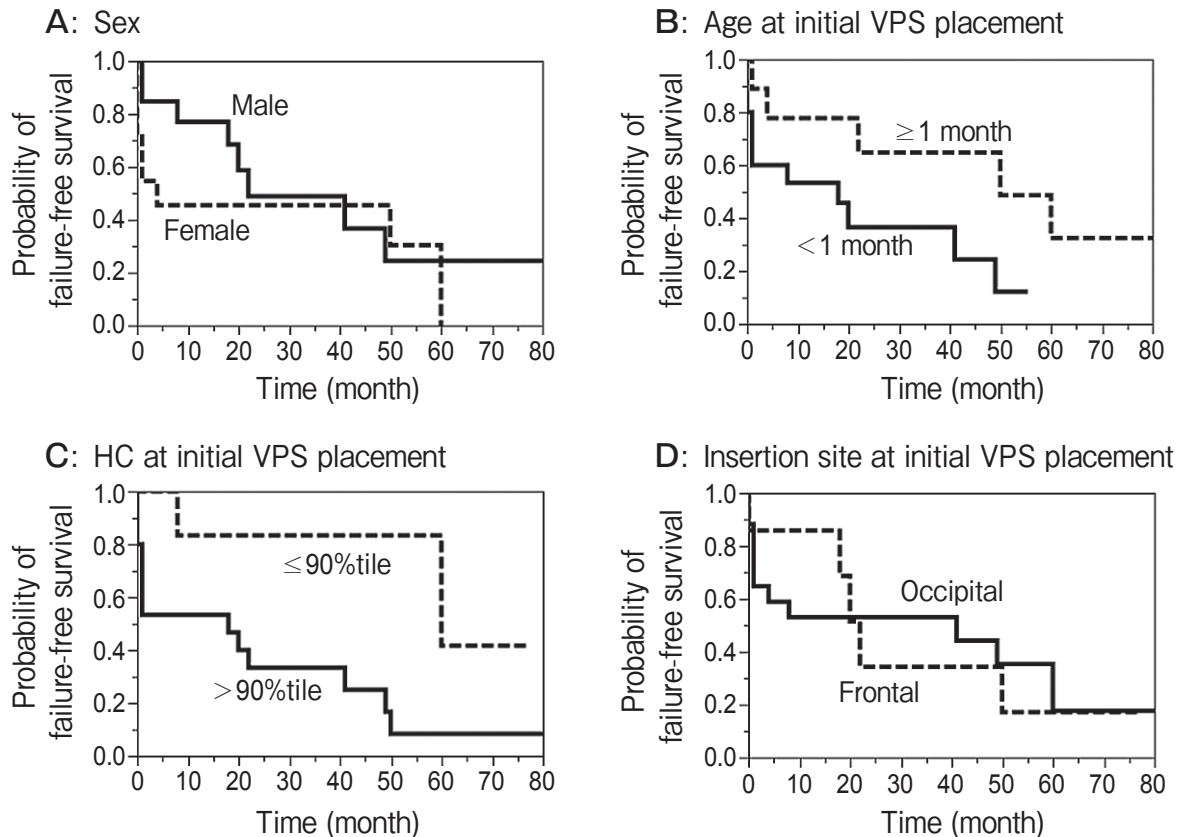


Fig. 3 Kaplan-Meier survival analysis for shunt failure. **A**, Failure-free curves categorized by sex. Solid line” males (n=13); dashed line” females (n= 11); **B**, Failure-free curves categorized by age at initial VPS placement. Solid line: < 1 month (n= 15); dashed line: ≥ 1 month (n= 9); **C**, Failure-free curves categorized by HC at initial VPS placement. Solid line: HC > 90%tile (n= 15); dashed line: ≤ 90%tile (n= 7); **D**, Failure-free curves categorized by insertion site at initial VPS placement. Solid line: occipital insertion (n= 17); dashed line: frontal insertion (n= 7).

Table 2 Univariate Cox regression analysis for shunt failure

	HR	95%CI	p
Male	0.69	0.25–1.91	0.472
Age < 1 month	2.93	0.96–10.95	0.059
HC > 90%tile (n = 22)	4.46	1.20–28.91	0.023
Occipital insertion	1.01	0.36–3.20	0.991

Table 3 Multivariate Cox regression analysis for shunt failure

	Adjusted HR	95%CI	p
Male	0.15	0.03–0.57	0.006
Age < 1 month	17.56	2.69–202.82	0.001
HC > 90%tile (n = 22)	2.95	0.52–24.84	0.228
Occipital insertion	0.64	0.18–2.44	0.494

residential bacterial flora [9]. Etiological factors must also be considered. The main causes of hydrocephalus in the present study, dealing with infantile cases, were myelomeningocele (10 of 24, 42%) and aqueductal stenosis (6 of 24, 25%). Previous studies found the rates of children’s diseases requiring VPS to be: myelomeningocele (15.6%), aqueductal stenosis (8.0%), post-hemorrhage (24.8%), and brain tumor (18.1%) [14]. The disease spectrum of the present

study differed somewhat.

In their shunt infection rate study, Kulkarni *et al.* reported myelomeningocele, 4.6%; aqueductal stenosis, 12.5%; intraventricular hemorrhage, 17.5% and tumor, 9.5% [8]. McGirt *et al.* found myelomeningocele, 10.3%; idiopathic/congenital, 13.0%; intraventricular hemorrhage, 16.7%; and tumor, 3.3% [10]. From these reports, we could not say that myelomeningocele was a risky etiology. Our Kaplan-

Meier analysis results indicated that the HC > 90% tile was also an important factor for shunt failure. Out of 15 patients shunted at < 1 month, there were 11 patients in the HC > 90% tile, and 10 shunt failures occurred afterwards. Clinicians should therefore exercise even greater care for patients who need a VPS at < 1 month of age when they are in the HC > 90% tile.

A previous study showed male preponderance in shunt failure [2], but that study included adult patients. Other studies dealing with children showed that the male risk ratios were 1.24 (95%CI: 0.63–2.47) [9] and 1.14 ($p = 0.5337$) [15]. These data indicate that there was no significant difference between the male and female patients. Although our present sensitivity analysis showed that female sex might be a risk factor for shunt failure, we were unable to find any reports of female preponderance.

The present rates of shunt failure [1–4] and shunt infection [6–13] were within the range found by previous studies. One of our patients with infection experienced CSF leakage, a risk factor for infection [8]. Both of the present patients with infection experienced fever at the beginning of the infection, an important sign of increased risk. The cause of infection in both cases was coagulase-negative Staphylococci, which was cultured from a preoperative skin culture. Although prophylactic antibiotics can be administered intravenously in such cases, one report described the injection of prophylactic vancomycin into the ventricle [2].

Both of our migration cases had CSF leakage. Many hypotheses have been reported regarding the upward migration of distal shunt tubing. One of them is the “windlass effect,” in which granulation tissue or a valve placed below the scalp acts as an anchoring point and the patient’s repeated head motion allows the distal tubing to be pulled in a proximal direction [16]. Shamsavaran *et al.* described a case in which subgaleal CSF collected in the suction catheter [17]. Subcutaneous fluid collection might be a risk factor for migration.

Insertion to the inferior horn could happen during tube insertion via the occipital site. Parieto-occipital entry was also indicated as a risk factor ($p = 0.09$) [3]. The results of the present study, however, showed no significant difference in risk between frontal and occipital insertions.

The rate of intracranial hemorrhage in previous reports was 1.1%–4% [18–20]. The intracranial hemorrhage rate in the present study (3 of 24 patients, 13%) was markedly higher. Hemorrhage may be caused by multiple attempts at perforation of the ventricles, puncture of the choroid plexus, or improper placement of the tubing within the parenchyma of the brain [18]. The rate of HC reduction was high among the present cases with hemorrhages, although this parameter has not yet been investigated fully. The rapid excretion of CSF may cause a rapid decrease in intracranial pressure, and rapid HC reduction should be closely monitored.

The primary limitations of this study were its small sample size, inadequate statistical analysis, and different spectrum of related diseases. Thus, each case was evaluated independently, in addition to the overall statistical analysis.

In conclusion, the results of this study revealed that the risk factors for shunt failure include age < 1 month at the initial VPS placement. The HC > 90% tile at the initial VPS placement could also be an important factor. Although there was not a high rate of shunt failure in this patient series, each infant must be treated according to his or her risk factors.

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