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[Instrumentation Assessments]

Randomized Trial of Cerebrospinal Fluid Shunt Valve Design in Pediatric Hydrocephalus

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Abstract

OBJECTIVE: Forty percent of standard cerebrospinal fluid shunts implanted for the treatment of pediatric hydrocephalus fail within the first year. Two new shunt valves designed to limit excess flow, particularly in upright positions, were studied to compare treatment failure rates with those for standard differential-pressure valves.

METHODS: Three hundred-forty-four hydrocephalic children (age, birth to 18 yr) undergoing their first cerebrospinal fluid shunt insertion were randomized at 12 North American or European pediatric neurosurgical centers. Patients received one of three valves, i.e., a standard differential-pressure valve; a Delta valve (Medtronic PS Medical, Goleta, CA), which contains a siphon-control component designed to reduce siphoning in upright positions; or an Orbis-Sigma valve (Cordis, Miami, FL), with a variable-resistance, flow-limiting component. Patients were monitored for a minimum of 1 year. Endpoints were defined as shunt failure resulting from shunt obstruction, overdrainage, loculations of the cerebral ventricles, or infection. Outcome events were assessed by blinded independent case review.

RESULTS: One hundred-fifty patients reached an endpoint; shunt obstruction occurred in 108 (31.4%), overdrainage in 12 (3.5%), loculated ventricles in 2(0.6%), and infection in 28 (8.1%). Sixty-one percent were shunt failure-free at 1 year and 47% at 2 years, with a median shunt failure-free duration of 656 days. There was no difference in shunt failure-free duration among the three valves ($P = 0.24$).

CONCLUSION: Cerebrospinal fluid shunt failure, predominantly from shunt obstruction and infection, remains a persistent problem in pediatric hydrocephalus. Two new valve designs did not significantly affect shunt failure rates.

The often exasperating inability of cerebrospinal fluid (CSF) shunts to provide continuous, problem-free, CSF diversion in pediatric hydrocephalus is well known. Previous reports indicated that the 1-year failure rate of CSF shunts is approximately 40% [1,14,19]. The result has been a myriad of modifications to the original shunt valve design (which was introduced more than 4 decades ago)[12], in attempts to improve treatment results. Two novel valve designs, i.e., the Orbis-Sigma valve (Cordis, Miami, FL) and the Delta valve (Medtronic PS Medical, Goleta, CA), were recently introduced and have been widely used, based on reports of reduced shunt failure in uncontrolled series [10,17,18]. Both designs differ from the original "standard" valve design in limiting the tendency to overdrain with upright posture.

Although shunt gravitational effects with upright postures are obviously greater in adults, overdrainage complications occur in children with approximately equal frequency [13,16,19]. The Orbis-Sigma valve was designed in a pediatric center, from which were issued the original data supporting its clinical efficacy [17]. The antisiphon device, which functions in a fashion equivalent to that of the Delta valve, has been specifically recommended for children [20]. Both new valve designs are quite appropriate for use in children, and it is sensible to implant, at the beginning of treatment, a valve that can address long-term complications.

Standard CSF shunt valves control unidirectional CSF flow by means of valve leaflets or their equivalent [6]. Typical valve configurations are ball-in-spring, diaphragm, miter, and slit valves. The valves open at a pressure differential across the valve that is determined by the valve characteristics and is designated as low, medium, or high(typically 5, 10, and 15 cm H_2O, respectively) [6,8,15,21]. Once open, the valves provide very little resistance to flow, so that the gravitational effects of upright postures lead to high flow rates and large negative intracranial pressures, termed "siphoning" [2,9]. The Delta valve(Medtronic PS Medical) reduces this tendency by adding a siphon-control device distal to a standard diaphragm valve. The siphon-control device consists of paired flexible diaphragms, which narrow an orifice as the shunt pressure becomes negative, thus reducing the flow [10]. The Delta valve is available in three opening pressure designations, i.e., Levels 1, 1.5, and 2 (7, 10.5, and 12 cm H_2O, respectively). The Orbis-Sigma valve (Cordis) limits flow by progressively narrowing the flow orifice with increasing pressure, as a pressure-sensitive ring moves along a variable-diameter rod. It has a single opening pressure of approximately 5 cm H_2O [18]. A randomized trial of these three valve designs was conducted to evaluate their respective failure rates.

PATIENTS AND METHODS

The details of the trial design have been previously reported [4,5]. The key features are summarized below.

Eligibility

The study was approved by the local institutional review board or its equivalent at each center. Before entering the study, each participating center was required to have placed at least five shunts of each valve design. To be eligible for the trial, patients were required to give informed consent(patients or their parents or designated guardians); be between birth and 18 years of age; have newly diagnosed hydrocephalus with documented cerebral

ventriculomegaly in computed tomographic, magnetic resonance imaging, or ultrasonographic imaging scans; and require a first ventriculoperitoneal CSF shunt insertion.

Patients were excluded if they had one of the following: 1) a previous indwelling CSF shunt (patients with subcutaneous reservoirs for aspiration or ventricular catheters draining externally or to the subcutaneous scalp were eligible), 2) active abdominal or CSF infection, 3) diffuse spread of tumor in the subarachnoid space, 4) marked prematurity with thin skin at risk for erosion from shunt hardware, 5) systemic disorders precluding CSF shunt insertion, 6) septated loculations within the ventricular system requiring more than one shunt, 7) a Dandy-Walker malformation, 8) an arachnoid cyst as a cause of hydrocephalus, or 9) an inability to be monitored for 1 year. Baseline data were collected for all eligible nonrandomized patients.

Randomization

Patients were randomized to one of the three valve designs (standard valve, Delta valve, or Orbis-Sigma valve), after induction of anesthesia, by the drawing of consecutive opaque envelopes located in each operating room. A standard valve was deemed to be any differential-pressure valve without any other flow-modifying device. For the standard and Delta valve groups, surgeons were allowed to choose whichever opening pressure they wished (the Orbis-Sigma valve had only one opening pressure level). Patients were stratified by center and by age (less than or more than 6 mo), and the randomization scheme was blocked with randomly varying block size.

Treatment

Patients underwent standardized history-taking, physical and neurological examinations, and laboratory tests, as well as imaging studies demonstrating enlarged ventricles. Ventricular size was measured as a modified Evan's ratio(an average of the maximal lateral width of the frontal and occipital horns divided by the maximal lateral diameter of the cranium)(7). The details of the surgical techniques and post-operative care were established according to the discretion of the surgeon and were recorded. These details included the prophylactic use of antibiotics, hair removal, the site of hardware insertion, the use of technical aids such as ventriculoscopes, hardware configurations, opening pressure designations for the standard and Delta valves, and postoperative head elevation or compressive dressings. Suggestions from the manufacturers for insertion techniques were solicited at the beginning of the trial and were distributed to all participating centers.

Follow-up monitoring

Study surgeons completed postoperative assessments, as well as follow-up assessments at 3 and 12 months and annually thereafter for up to 3 years. All patients presenting with suspected shunt malfunctions underwent standardized history-taking and physical examinations, as well as appropriate investigational tests, including brain imaging and CSF sampling for infection. If the patients underwent subsequent surgery, standardized operative findings plus the type and site of shunt malfunction were recorded.

Outcome events

The primary outcome event was shunt malfunction. There were four subtypes of shunt malfunctions-shunt obstruction, overdrainage, loculated ventricles, and infection. Detailed criteria were established for each subtype and were published previously (5). Determination of an endpoint event occurred before the patient was returned to the operating room, although the surgical findings were used as confirmatory evidence. The methodology center was

notified when a probable endpoint occurred. Patient eligibility and endpoints were blindly adjudicated, and any discrepancies were referred to an external blinded adjudication committee not otherwise involved in the trial. Secondary outcome events included death, surgical complications, type of shunt malfunction, site of shunt obstruction, and hospital stay.

Statistical analysis

Sample size calculations were based on a reduction in the 1-year failure rate from 40 to 20%, with independent comparisons of the three valves with Type I ([alpha]) error set to 0.017 (0.05/3) and Type II ([beta]) error set to 0.2. This resulted in an estimated sample size of 115 patients/group, using two-tailed tests. Time to shunt failure was compared among the three groups by log-rank tests. Baseline variables and secondary outcomes were compared using descriptive statistics, including 95% confidence levels. Deaths and surgical complications were assessed blindly at the midpoint of accrual, to ensure safety.

RESULTS

Patients

Between October 1, 1993, and October 31, 1995, 367 patients were randomized. Twenty-three were ruled ineligible (after randomization) by blinded adjudication, leaving a total of 344 eligible randomized patients. Eight patients did not complete the minimum 1-year follow-up period. The baseline characteristics of the 344 patients are shown in Table 1. Most were neonates or infants at diagnosis, with a slight preponderance of boys. The common causes of hydrocephalus in this age group were represented, with intraventricular hemorrhage and myelomeningocele being the most frequent and approximately 10% being unknown. Clinical presentation reflected symptoms of raised intracranial pressure. Irritability, delayed developmental milestones, nausea and vomiting, lethargy, and headache were common symptoms. Increased head circumference, bulging fontanel, delayed development, loss of upward gaze ("sunsetting"), decreased levels of consciousness, and papilledema were common signs. Almost 20% of the patients had previously received a subcutaneous reservoir or external ventricular drain. Most patients exhibited severe hydrocephalus, as indicated by the ventricular volume index. The fourth ventricle was normal in size in two-thirds of the patients. There were no clinically important differences in baseline characteristics among the groups. The baseline characteristics of the 48 eligible and nonrandomized patients showed a slightly higher proportion of patients with brain tumors and aqueductal stenosis. These patients were suitable for third ventriculostomy and presumably underwent this procedure instead.

	Delta	Standard	Sigma
Demographics			
Number of patients	115	114	115
Gender (% boys)	55.7	61.4	49.6
Age (d)			
Mean	506.3	603.3	873.1
Median	73.0	78.0	89.0
Corrected age (d)			
Mean	504.3	603.2	568.6
Median	43.0	50.0	70.0
Gestational age (d)	36.6 ± 4.0	36.7 ± 4.8	36.5 ± 4.5
Birth weight (g)	2778.6 ± 848.3	2841.2 ± 1036.3	2853.8 ± 1131.0
Hydrocephalus cause			
Intraventricular hemorrhage (%)	19.1	25.9	28.1
Myelomeningocele (%)	24.3	24.1	15.8
Tumor (%)	8.7	8.0	10.5
Aqueduct stenosis (%)	7.8	8.0	5.3
Cerebrospinal fluid infection (%)	6.1	4.5	5.3
Head injury (%)	2.6	1.8	0.0
Two or more causes (%)	9.6	6.3	10.5
Other (%)	9.6	11.6	13.2
Unknown (%)	12.2	9.8	13.4
Symptoms			
Headache (%)	14.5	23.3	15.0
Nausea or vomiting (%)	16.7	18.3	22.0
Irritability (%)	22.9	30.9	25.9
Lethargy (%)	15.5	18.9	16.2
New seizures or change in seizure pattern (%)	2.8	7.3	9.7
Diplopia (%)	6.0	4.6	6.7
Fever (%)	2.7	4.8	0.9
Delayed developmental milestones (%)	18.6	19.3	21.3
Worsening school performance (%)	7.2	1.4	3.9
Signs			
Papilledema (%)	15.5	13.1	7.7
Bulging fontanelle (%)	67.3	72.1	72.5
Increased head circumference (%)	65.3	78.3	80.0
Decreased level of consciousness (%)	12.3	14.9	10.6
Nuchal rigidity (%)	2.6	1.8	0.9
Sixth nerve palsy (%)	5.6	2.8	5.5
Loss of upward gaze (%)	16.4	16.5	14.8
Hemiparesis (%)	6.1	4.4	0.9
Other focal neurological deficit (%)	12.3	12.5	12.4
Delayed developmental milestones (%)	18.3	20.0	24.5
Cutaneous signs of occult spinal dysraphism (%)	4.4	5.3	2.6
Other positive physical finding (%)	15.7	10.6	4.3
Previous surgery			
Subcutaneous reservoir (%)	6.1	6.1	2.1
Ventricular drain (%)	8.0	11.9	18.0
Preoperative imaging			
Preshunt ventricular volume index	0.57 ± 0.13	0.56 ± 0.11	0.57 ± 0.11
Transependymal edema (%)	27.8	27.2	24.3
Intraventricular blood (%)	5.7	13.9	11.6
Focal mass lesion present at shunt insertion (%)	8.7	11.4	13.0
Tumor (%)	2.6	6.1	6.1
Hematoma (%)	0.0	0.0	1.7
Other (%)	3.7	2.6	2.6

TABLE 1. Baseline Characteristics

Surgery

Pertinent surgical details are shown in Table 2. When patients were randomized to a standard valve, most surgeons selected a medium opening pressure; when patients were randomized to a Delta valve, most surgeons selected a Level 1 opening pressure. A two-piece shunt system with a separate ventricular catheter was the most common hardware configuration. Almost all patients received antibiotics (either a cephalosporin or methicillin) prophylactically before skin incision. Approximately 40% received additional antibiotic doses. Approximately two-thirds of patients had their scalp hair shaved, with the rest having the hair clipped or undergoing no hair removal at all. Most surgeons chose an occipital entry site, directing the catheter to either the frontal or occipital horn on the

same side. Slightly more than 20% used the assistance of endoscopy, ultrasonography, or plain x-rays to position the ventricular catheter. For 90% of patients, the ventricular catheter was satisfactorily placed on the first attempt. Almost all surgeons passed the peritoneal catheter down the anterior chest wall. It was placed in the abdomen slightly more often under direct observation than with a trochar. The average operating time was slightly more than 30 minutes. Postoperative complications, other than the endpoint of infection, were extremely few and usually related to local wound problems. The median hospital stay ranged between 5 and 6 days. The only apparent difference in surgical techniques among the valves was that more patients with the Orbis-Sigma valve were treated with head elevation and a compressive scalp dressing, as was recommended by the Orbis-Sigma shunt manufacturer.

	Delta	Standard	Sigma
Valve selection details			
Valve opening pressures (%)			
Level 1 (~5 cm H_2O)	75.7		
Level 1.5 (~7.5 cm H_2O)	11.3		
Level 2 (~10 cm H_2O)	13.0		
Low (~5 cm H_2O)		22.3	
Medium (~10 cm H_2O)		73.4	
High (~15 cm H_2O)		6.5	
Shunt pieces (%)			
One piece	0.0	16.8	4.3
Two piece	75.4	55.8	93.0
Three piece	24.6	27.4	2.6
Prophylactic perioperative antibiotics (%)	99.6	92.0	91.3
Surgical details			
Cranial site hair removal (%)			
Shaved	70.4	65.8	67.6
Clipped	16.5	14.9	18.3
Neither	13.0	19.3	14.0
Head entry site (%)			
Coronal	16.5	14.9	16.3
Occipital	83.5	85.1	83.5
Ventricular catheter placement assistance (%)			
Endoscopy	7.0	7.1	8.8
Ultrasonography	7.0	13.3	13.0
X-rays	6.4	5.8	4.6
Ventricular catheter placed in first attempt (%)	92.9	89.3	88.7
Abdominal entry technique (%)			
Direct observation	60.9	63.1	54.8
Trochar	39.1	36.9	45.2
Additional surgical procedures (%)	16.7	20.2	14.3
Operating time			
Operating time (min)	36 ± 20	36 ± 21	35 ± 20
Minimum (min)	10	12	12
Maximum (min)	90	120	105
Postoperative care			
Head of bed elevated (%)	34.9	42.5	77.3
Compressive head dressing (%)	4.7	2.8	12.7
Postoperative complications			
Intracranial hemorrhage (%)	0.0	0.9	0.0
New or increased neurological deficit (%)	0.0	0.0	0.0
Neck injury (%)	0.0	0.9	0.0
Chest injury (%)	0.9	0.9	0.9
Abdominal injury (%)	0.0	0.0	0.0
Inadvertent skin perforation along shunt tract (%)	0.9	0.0	0.0
Wound dehiscence (%)	1.7	1.8	0.0
Postoperative subcutaneous fluid collection (%)	2.9	1.9	7.2
Transient wound cerebrospinal fluid leak (%)	0.0	0.9	0.9
Perioperative death (%)	0.9	0.0	0.0
Other complication (%)	6.1	7.9	4.3

TABLE 2. Surgery

Shunt failure

During the course of the trial, 150 (43.6%) of the patients met the primary endpoint of shunt failure, 108 (31.4%) with shunt obstruction, 12(3.5%) with overdrainage, 2 (0.6%) with loculated compartments, and 28 (8.1%) with infection (Fig. 1A). Nine patients died, four as a result of progression of neoplastic disease and the others as a result of hyponatremia, sepsis, progressive respiratory disease, gastroenteritis, or sudden infant death (with normal-size

ventricles observed in the autopsy). There were no deaths related to shunt failure. The clinical features and test results for patients with shunt failure are shown in Table 3. The clinical features of mechanical failure were those of elevated intracranial pressure. Signs specifically related to the shunt equipment included CSF tracking along the tubing and failure of the CSF reservoir to refill. Patients with shunt infections were often febrile, with signs of inflammation at the affected site, and yielded positive bacterial cultures. Forty-three percent of the infected shunts were also obstructed. Fever was very unusual with mechanical shunt failure alone. Most patients with mechanical shunt failure showed enlarging ventricles in computed tomographic or ultrasonographic scans. Disruption or migration of the shunt equipment was also frequently observed in plain x-rays. Shunt flow tests were necessary for only a few patients, and one patient underwent intracranial pressure monitoring to permit the diagnosis of shunt failure.

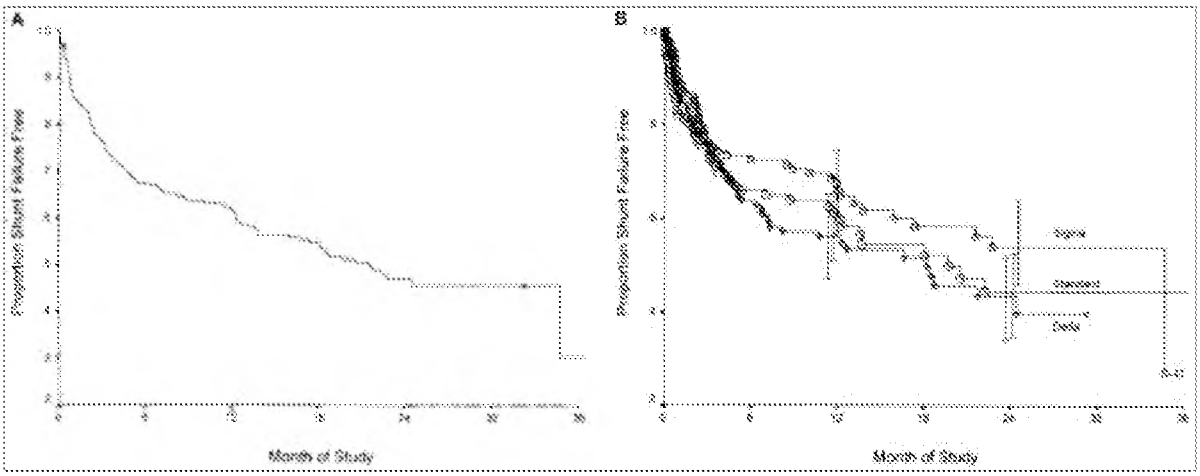

FIGURE 1. Kaplan-Meier curves for the shunt failure-free proportion, for all patients (*A*) and for the three valve designs (*B*). The three valve designs did not differ significantly (by log-rank test, $P = 0.24$). There were fewer than five patients in at least one group after 24 months.

	All (n = 148)	Mechanical Failure (n = 122)			Infection (n = 26)
		Delta	Standard	Sigma	
Symptoms					
Headache (%)	46.2	47.8	45.0	43.8	53.8
Nausea or vomiting (%)	39.3	44.4	42.5	28.1	30.8
Irritability (%)	35.8	37.8	40.0	28.1	34.6
New seizure or change in seizure pattern (%)	3.7	0.0	0.0	6.3	3.8
Delayed developmental milestones (%)	8.3	6.7	10.0	9.4	3.8
Worsening school performance (%)	3.7	2.2	0.0	3.1	0.0
Abdominal pain (%)	3.3	0.0	0.0	0.0	19.2
Signs					
Papilledema (%)	2.6	4.4	0.0	3.1	3.8
Bulging fontanelle (%)	42.7	33.6	55.0	37.5	53.1
Increased head circumference (%)	38.5	37.8	45.0	31.3	38.2
Decreased level of consciousness (%)	18.8	22.2	20.0	12.5	7.7
Nuchal rigidity (%)	0.8	0.0	0.0	0.0	3.8
Sixth nerve palsy (%)	2.6	0.0	5.0	3.1	3.8
Loss of upward gaze (%)	6.0	11.1	2.5	3.1	0.0
Fluid tracking along shunt (%)	23.1	17.8	12.5	43.8	15.4
Cerebrospinal fluid leak necessitating shunt revision (%)	3.4	0.0	2.5	9.4	15.4
Shunt reservoir cannot be depressed (%)	5.1	6.7	0.0	9.4	3.8
Shunt reservoir does not refill (%)	12.0	11.1	15.0	6.3	0.0
Fever (%)	2.6	0.0	0.0	0.0	69.2
Meningismus (%)	1.3	0.0	0.0	0.0	8.0
Wound erythema (%)	4.9	0.0	0.0	0.0	26.9
Skin erosion (%)	4.2	0.0	0.0	0.0	23.1
Purulent wound discharge (%)	1.4	0.0	0.0	0.0	7.7
Abdominal mass (pseudocyst) (%)	0.7	0.0	0.0	0.0	3.8
Peritonitis (%)	2.8	0.0	0.0	0.0	15.4
Test results					
Enlarging ventricles (%)	70.9	64.4	77.5	71.9	30.8
Image type (%)					
Ultrasonography	13.7	11.1	12.5	18.8	15.4
Computed tomography	79.5	86.0	80.0	68.6	61.5
Magnetic resonance imaging	3.4	4.4	2.5	3.1	0.0
None	3.4	4.4	0.0	6.3	26.9
Disruption/migration of shunt in x-rays (%)	13.7	11.1	15.0	15.6	0.0
Shunt flow study showing obstruction (%)	2.6	2.2	0.0	6.3	0.0
Elevated intracranial pressure (%)	0.0	0.0	2.2	0.0	0.0
Shunt tap, no aspiration possible (%)	3.4	2.2	7.5	0.0	0.0
Shunt tap, high pressure (%)	0.9	0.0	2.5	0.0	7.7
Shunt tap, relief of symptoms (%)	3.4	0.0	7.5	3.1	7.7
Positive bacterial culture of cerebrospinal fluid and/or shunt material (%)	16.9	0.0	0.0	0.0	92.3

TABLE 3. Shunt Failure Presentation

The overall percentage of patients who were free of shunt failure was 61% at 1 year and 47% at 2 years, with a median shunt failure-free duration of 656 days. There were no differences among the three shunt valve groups, either by log-rank tests for equality of the three curves (log rank = 2.90, $P = 0.24$) or by individual pairwise comparisons (Fig. 1B). There seemed to be some center variability in shunt survival, as shown in Figure 2. However, a Cox regression model adjusted for failure cause, patient age, ventricular size, and center also failed to show any significant differences among the valves. The median time to mechanical failure was 99 days and that to infection was 23 days.

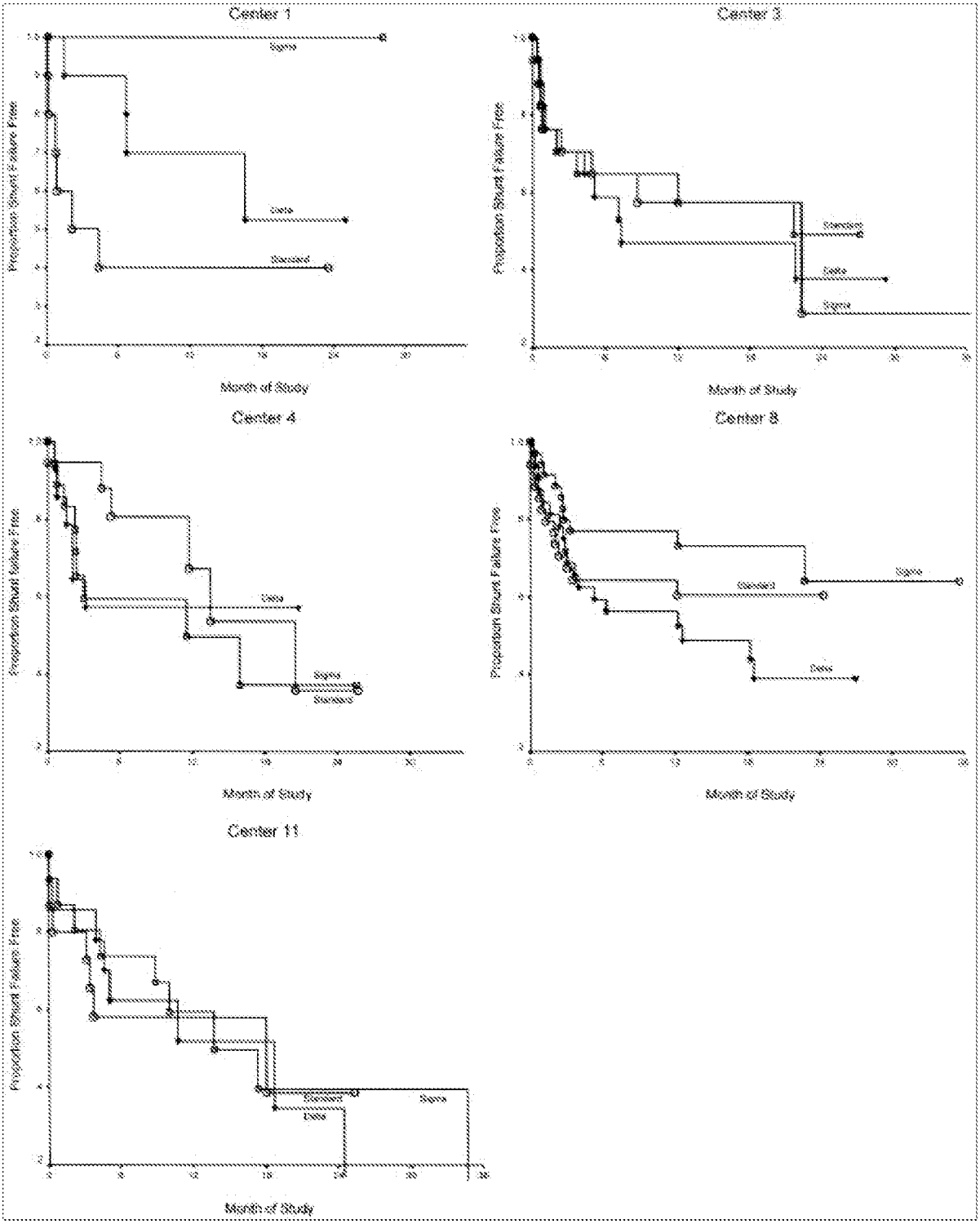

FIGURE 2. Kaplan-Meier curves for the shunt failure-free proportion after shunt insertion at a major center (> 25 patients entered).

The primary endpoint subtypes for each valve are shown in Table 4, along with the secondary endpoint of site of shunt obstruction. The total shunt obstructions were 38, 39, and 31 in the Delta, standard, and Orbis-Sigma valve groups, respectively; when distributed by site, there were 16, 18, and 2 ventricular catheter obstructions, respectively. There were 9, 3, and 0 failures resulting from shunt overdrainage in the Delta, standard, and Orbis-Sigma valve groups, respectively. Failure rates and mechanisms seemed similar within specific age subgroups (<=2 yr versus >2 yr).

	No. of Cases		
	Delta	Standard	Sigma
Main endpoints, all patients	115	114	115
Shunt obstruction	38 (33.0%)	39 (34.2%)	31 (27.0%)
Overdrainage	9 (7.8%)	3 (2.6%)	0 (0.0%)
Loculated compartments	0 (0.0%)	0 (0.0%)	2 (1.7%)
Shunt infection	9 (7.8%)	7 (6.1%)	12 (10.4%)
Secondary endpoints, shunt obstruction site	38	39	31
Ventricular catheter	16 (42.1%)	18 (46.2%)	2 (6.5%)
Valve	2 (5.3%)	5 (12.8%)	8 (25.8%)
Peritoneal catheter	5 (13.2%)	2 (5.1%)	2 (6.5%)
Distal valve or peritoneal catheter	2 (5.3%)	1 (2.6%)	5 (16.1%)
Shunt migration disconnection	3 (7.9%)	7 (17.9%)	7 (22.6%)
Ventricular catheter plus other site	6 (15.8%)	1 (2.6%)	0 (0.0%)
Unknown	4 (10.5%)	5 (12.8%)	7 (22.6%)
Main endpoints, patients of >2 yr*	39	39	38
Shunt obstruction	8	3	4
Overdrainage	3	1	0
Loculated compartments	0	0	0
Shunt infection	0	1	2

* Mean age, 7.7 years; median age, 6.3 years; range, 2–17 years.

TABLE 4. Endpoints

DISCUSSION

In major pediatric neurosurgical centers in North America and Europe, shunt failure rates are particularly high in the first 6 months, followed by a persistent but lower failure rate in the next 2 years. The early 6-month failures occur from both shunt infection and mechanical failure. The subsequent failures are predominantly mechanical, because shunt infection is uncommon after the first 6 months.

No significant differences in the proportions of patients who were shunt failure-free were observed among the three valve designs. These valves represent the cumulative results of shunt valve research and development in the past 30 years. The newer valves (Delta and Orbis-Sigma valves) were specifically designed to prevent overdrainage in upright postures and to result in more physiological drainage of CSF. It had been hypothesized that the reduced tendency for CSF to siphon into the ventricular catheter in upright positions accounted for the reduced failure rates in uncontrolled series using the Delta and Orbis-Sigma valves (10,17,18). In this study, there were few ventricular catheter obstructions with the Orbis-Sigma valve and no failures resulting from over-drainage. This suggests that valve design can have important effects on the shunt failure mode. Nevertheless, obstructions occurred at other sites along the Orbis-Sigma shunt, including the valve. It seems that the CSF dynamics of shunted hydrocephalus are complex and not optimally treated by current valve designs. Further research is needed to optimize shunt valve design.

It can be argued that the different types of standard valves (e.g., diaphragm valve or ball-in-spring valve), using various opening pressure levels and made by various manufacturers, in this study do not constitute a single valve design group. Similarly, the choice by the surgeon of a particular Delta valve level may have been inappropriate for a patient from a particular age group. Although bench testing has demonstrated mechanical differences among the various standard valves, these observations have not translated into clinically important differences; in uncontrolled series at different centers using a variety of standard valves, the results were very similar (1,14,19). Given that the overall results of this trial failed to show any differences among three very different valve designs, it is unlikely that any change in the standard valve mechanism or opening pressure or the Delta valve level chosen would have any significant effect on the outcome of this study.

The infection rate of 8.1% observed in the present study is higher than that recently reported from one particular center (0.7%)[3] but is certainly within the range reported in other controlled and uncontrolled series [11]. Some of the variability in published infection rates may be the result of varying definitions of shunt infection. The infection rate in this randomized trial was determined by use of a specific definition of infection [5], applied in a prospective consistent manner and subject to blinded adjudication.

A higher proportion of eligible nonrandomized patients (compared with the study participants) exhibited characteristics that indicated suitability for third ventriculostomy. We suspect that patients suitable for third ventriculostomy were not entered into the trial and may be poorly represented in the study sample. Therefore, the results may not apply to these patients. With this exception, the study results should be reasonably applicable to the population of children in North America and Europe who require a CSF shunt for the first time.

The median age of the patients in the study was quite young, and the study does not have the power to assess the different valve designs within specific age groups. However, secondary analysis does not suggest that the results might be different in older children, who are ambulatory and for whom shunt overdrainage or siphoning is at least conceptually more important (Table 4). The causes of hydrocephalus in adults are different, as might be the function of these particular valve designs, so that the results of this trial should not be extrapolated to adult patients.

New shunt valve designs, based on more sophisticated or "physiological" control of CSF drainage, have been introduced as a solution to the generally recognized poor results obtained with CSF shunts. Claims of improved efficacy have been drawn from uncontrolled patient series, and these devices have come into widespread use after approval by the Food and Drug Administration. The cost of these new valves can be up to 10 times that of some valves of standard design. This is the first randomized trial to examine shunt valve design and is one of the few neurosurgical device trials. Based on this randomized trial, we cannot recommend one valve design over another for children with newly diagnosed hydrocephalus. Shunt valve design may still be a very important issue in reducing shunt obstruction, but clearly more research is needed into the complexities of CSF and brain fluid dynamics and biomechanics. Shunt infection also remains a persistent and unsolved problem.

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APPENDIX

The following persons and institutions participated in the pediatric shunt design trial: Co-principal Investigators and Steering Committee members, James M. Drake, M.B., B.Ch. (Hospital for Sick Children, Toronto, Canada), and John R.W. Kestle, M.D. (Center for Evaluation Sciences, British Columbia's Children's Hospital); other Steering Committee members, Doug Cochrane, M.D. (British Columbia's Children's Hospital), Ruth Milner, M.Sc.(British Columbia's Children's Hospital), and Nancy MacNeil, B.N. (British Columbia's Children's Hospital); additional members of the Executive Committee, Stephen Haines, M.D., Steven J. Schiff, M.D., Joseph Piatt, Jr., M.D., Christian

Sainte-Rose, M.D., Frederick Boop, M.D., and Paul Steinbok, M.D; members of the Adjudication Committee, Ken Poskitt, M.D. (Division of Neuroradiology, British Columbia's Children's Hospital), Liliana Goumnerova, M.D. (Division of Neurosurgery, Children's Hospital, Boston, MA), and A. Leland Albright, M.D. (Division of Neurosurgery, Children's Hospital of Pittsburgh, Pittsburgh, PA). The participating centers (in order of the number of eligible patients entered) and investigators were as follows: Hôpital Necker Enfants Malades (Paris, France), Christian Sainte-Rose, M.D., Giuseppe Cinalli, M.D., Alain Pierre-Kahn, M.D., Dominique Renier, M.D., and Michel Zerah, M.D.; The Hospital for Sick Children, James Drake, M.B., B.Ch., James Rutka, M.D., Robin Humphreys, M.D., Harold Hoffman, M.D., and Maria Lamberti-Pasculi, R.N. (data coordinator, nurse specialist); Arkansas Children's Hospital (Little Rock, AR), Frederick Boop, M.D., Charles Teo, M.D., Bruce Cherny, M.D., and Sharon Aureli, R.N. (data manager, nurse specialist); British Columbia's Children's Hospital, John Kestle, M.D., Douglas Cochrane, M.D., and Paul Steinbok, M.D.; Oregon Health Sciences University (Portland, OR), Joseph Piatt, Jr., M.D.; Utrecht University(Utrecht, The Netherlands), Peter Vandertop, M.D., and S. Broomstra, M.D.; Children's National Medical Center (Washington, DC), Steven Schiff, M.D., William Chadduck, M.D., and David Donahue, M.D.; University of Minnesota(Minneapolis, MN), Stephen Haines, M.D., and Walter Hall, M.D.; University of Mississippi Medical Center (Jackson, MS), Andrew Parent, M.D.; St. Justine Hospital, Montreal (Quebec, Canada), Andre Turmel, M.D., and Claude Mercier, M.D.; Alberta Children's Hospital (Calgary, Canada), Terence Myles, M.D., and Mark Hamilton, M.D.; Children's Hospital of Alabama (Birmingham, AL), Jerry Oakes, M.D., and Tim Mapstone, M.D.

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Key words: Cerebrospinal fluid; Cerebrospinal fluid shunts; Hydrocephalus; Randomized controlled trial

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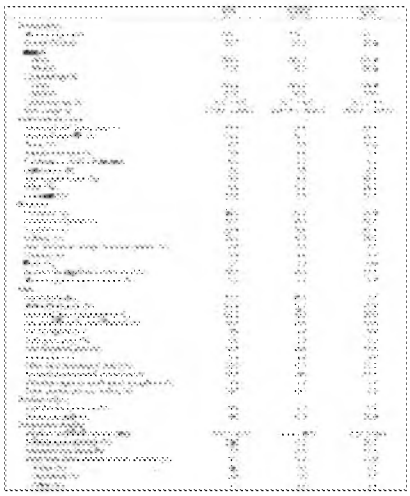

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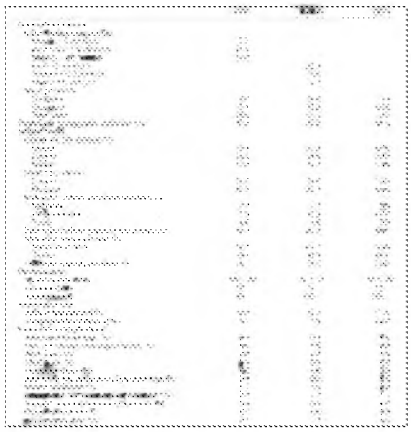

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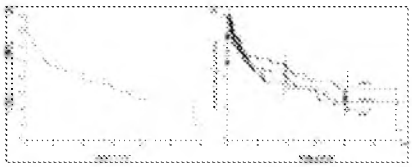
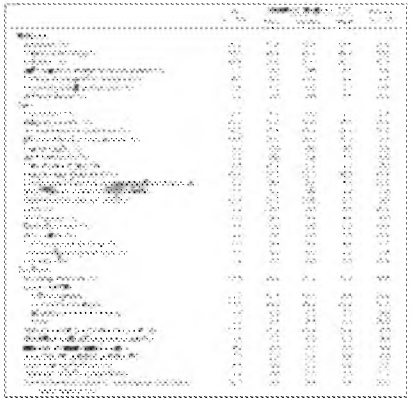


Figure 1



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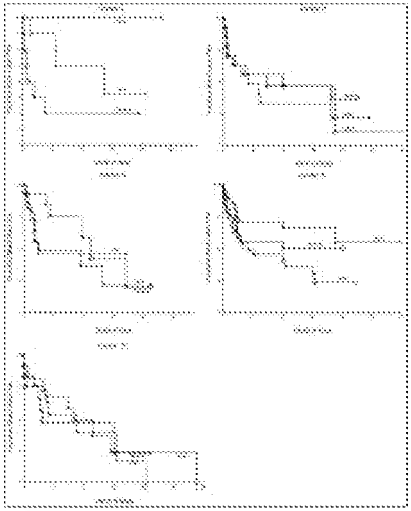

Figure 2

Table 4