Original Paper

Pediatric Neurosurgery

Pediatr Neurosurg 2005;41:186–191
DOI: 10.1159/000086559

Received: October 19, 2004
Accepted after revision: April 10, 2005

Long-Term Survival of Individuals with Myelomeningocele

Beth Ellen Davis[a, b] Colleen M. Daley[b] David B. Shurtleff[b] Sharon Duguay[b]
Kristy Seidel[b] John D. Loeser[b] Richard G. Ellenbogen[b]

[a]Department of Pediatrics, Madigan Army Medical Center, Tacoma, Wash., and [b]Departments of Pediatrics and Neurological Surgery, University of Washington, Seattle, Wash., USA

Key Words
Myelomeningocele · Survival · Shunts

Abstract
The objectives of this study were to extend survival analysis into adulthood for patients with myelomeningocele (MM) and to compare survival curves for patients born with varying defect severity before and after 1975. We have reviewed existing data for 904 patients with MM seen in a large multidisciplinary children's clinic over 43 years. Before 1975, a major contributor to decreased survival is death during infancy. The presence of cerebral spinal fluid shunting is a major contributor to increased survival. After 1975, survival to adolescence is similar regardless of shunt status ($p = 0.17$). For all patients alive at age 16, a significant decrease in survival probability after age 34 years was found for individuals with shunted hydrocephalus compared to those without a shunt ($p = 0.03$). Although childhood survival for individuals born after 1975 is not related to shunt status, adults with MM and shunted hydrocephalus may be at risk for decreased longevity.

Introduction

Myelomeningocele (MM) remains the most common central nervous system birth defect in the United States, despite a consistently decreasing birth prevalence and lesion severity over the past 10 years [1, 2]. The decline has been attributed to many factors, including improved maternal nutrition and folate supplementation, and availability of prenatal screening, diagnosis, and options for continuation of pregnancy. During the same time frame, the prevalence of adolescents and adults with MM has significantly increased secondary to increased longevity throughout childhood. Childhood survival data from our institution increased from 60% in 1960 to 90% in 1985 [3]. Improved childhood survival appears to have many contributors including prenatal referral to tertiary care centers, prophylactic minimization of birth trauma, widespread application of cranial computerized tomography and ultrasonography, early recognition of progressive hy-

The opinions or assertions contained herein are the private views of the authors and are not to be construed as official or reflecting the views of the Department of the Army or the Department of Defense.

KARGER

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

1016–2291/05/0414–0186$22.00/0

Accessible online at:
www.karger.com/pne

Beth Ellen Davis, MD, MPH
3715 Brookside Way West
University Place, WA 98466 (USA)
Tel. +1 253 566 0944 (home), +1 253 968 0253 (work)
Fax +1 253 958 5586, E-Mail BethEllen.Davis@nw.amedd.army.mil

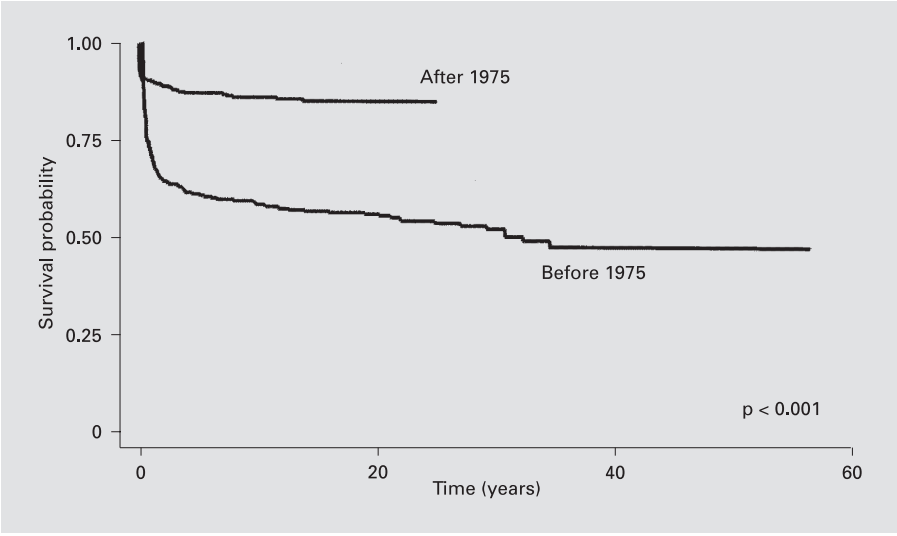

Fig. 1. Survival among all patients, grouped by birth date before 1975 and after 1975 (n = 904).

drocephalus, improved technology in cerebral spinal fluid (CSF) shunting, and broad-spectrum antibiotics.

For the above reasons, some experts in the field have proposed that MM is a 'new disease', since the mid-seventies [4]. There are, however, limited reports of life expectancy for adults with MM [5–9]. Previous studies have reliably plotted survival through 10–15 years of age [5, 8, 9]. Furthermore, there is scant documentation to separate life expectancy predictions based on vastly improved medical management strategies implemented in the 1970s [3], which would apply to the current national population of adolescents and young adults with MM. The purpose of this study was to extend survival analysis for patients with MM into adulthood and to compare survival curves for patients born with varying severity of defects before and after 1975.

Methods

We reviewed existing data on 904 patients with MM seen in the regional multidisciplinary birth defects clinic at Children's Hospital and Regional Medical Center and the University of Washington Medical Center of Seattle, Wash., USA, from 1957 until 2000. This sample represents 86% (904/1,054) of all patients with MM seen and entered into the clinical database during this time period.

Morbidity and mortality data were abstracted from the computerized clinical database, Patient Data Management System (PDMS/fx) [10], containing prospectively collected patient information for Birth Defects Clinic visits and adolescent/adult health status. Ongoing quality assurance of patients' health status was maintained through patient-initiated contacts, primary care provider consultation, subspecialty updates, infrequent counseling appointments, and telephone surveillance. Recent efforts had previously been made to telephonically locate patients not in contact with one of the authors (D.B.S.) in the last 2 years to update health status. The data were transferred to Intercooled STATA for estimation of aggregate survival by Kaplan-Meier life survival curves and single time point analysis testing. Age 16 years was chosen for time point analysis to reflect age of mid-adolescence. It also captured patients who were uniformly eligible to receive care in a regional multidisciplinary pediatric clinic before transitioning to individual adult care systems.

One hundred and fifty patients were excluded from the analysis secondary to patient information indicating a single clinic visit during infancy (most of these patient visits represented consultation from Pacific Islands, or second opinions from outlying regions).

Main outcome measures included patient variables relevant to survival such as birth date, presence of severe hydrocephalus at birth, CSF shunting for progressive hydrocephalus, clinically insignificant hydrocephalus at birth, gender, evidence of other congenital defects at birth, and prematurity (<34 weeks of gestation). Human subjects review was fulfilled through Children's Hospital and Regional Medical Center Institutional Review Board, Seattle, Wash., USA.

Results

Participants' age ranged from 0 to 83 years. There were 454 (50.2%) females. Four hundred and twelve patients were born and treated before 1975, 113 of whom have died (27%) with 54% survival to 16 years of age. Thirty-nine of 494 patients with birth dates after 1975 have died (8%) with an 85% survival to 16 years of age. The data support improved survival probability ($p < 0.001$, 95% CI for the difference 0.15–0.25 [11]) for patients with MM born after 1975 (fig. 1).

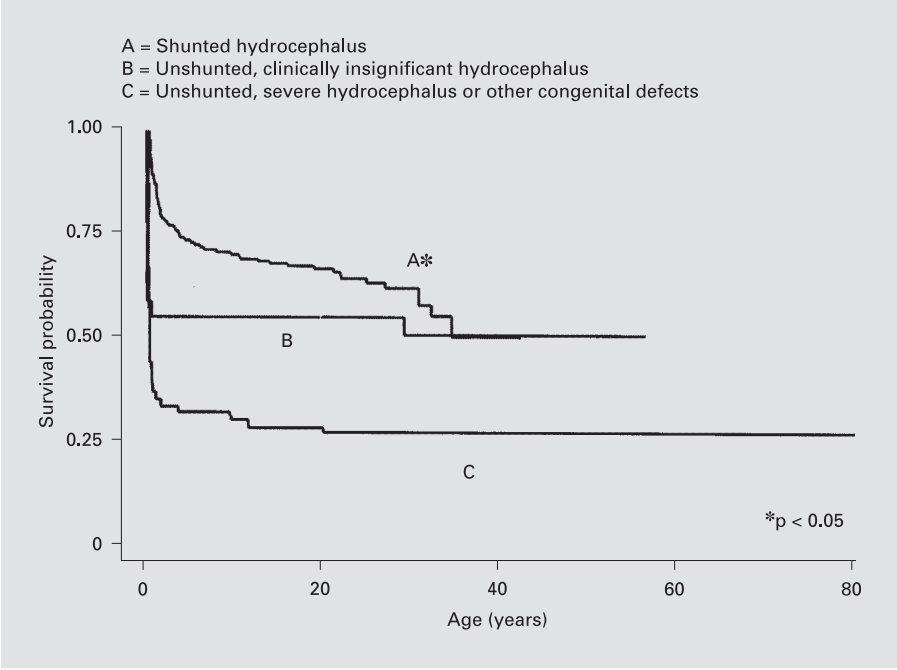

Fig. 2. Survival among patients born and treated before 1975 (n = 412). Group A (n = 250), group B (n = 62), group C (n = 100). Group A has significantly higher survival probability in childhood compared to groups B and C, as marked by an asterisk. The x-axis extends from birth to 83 years.

For the cohort born before 1975, 250 individuals (61%) underwent MM back closure and CSF shunting for progressive hydrocephalus at some point in their life, most often during infancy. These patients are identified as group A in figure 2. Sixty-eight percent survived to 16 years of age. Of the unshunted MM patients born before 1975, 62 (15%) underwent MM closure, had normal head circumferences at birth, did not demonstrate evidence of progressive hydrocephalus during infancy, were full term (>35 weeks of gestation), and did not have other congenital anomalies (e.g. congenital heart defect, chromosomal abnormality, severe microcephaly) and are represented in figure 2 as group B. The survival probability is 55% for these patients to age 16 years. The remaining 100 (24%) unshunted MM patients born before 1975 were given an extremely poor prognosis [3, 5, 12] secondary to 'unshuntable' hydrocephalus at birth (central nervous system infection or bleeding preventing CSF shunting), or additional birth defects complicating medical management. A few families withheld surgical repair for religious or social reasons. Combined, this group received supportive care only, and is labeled group C in figure 2. Survival at 16 years of age is 28%. Having a shunt in place (group A with a survival of 68%) predicted a better life expectancy to adulthood ($p < 0.05$) than the unshunted condition (groups B and C, with survivals of 55% and 27%, respectively) by age 36 for individuals born before 1975. This age was chosen because it was the last age to contain 5 or more individuals in each group for comparison.

For the cohorts born after 1975, the same criteria identified a shunted group of patients with MM (group A, n = 401, 82%), an unshunted, clinically insignificant hydrocephalus group of patients with MM (group B, n = 56, 11%), and an unshunted group of MM patients with severe or additional birth defects, who were managed supportively (group C, n = 35, 7%). Survival probabilities for these three groups are presented in figure 3. Groups A, B and C after 1975 have individual survival probabilities at age 16 of 90, 83 and 58%, respectively, and significantly exceed the corresponding probabilities for groups before 1975 ($p < 0.001$). Additionally, both groups A and B survive significantly better than group C ($p = 0.03$) as would be expected given improved surgical techniques, improved antibiotic coverage, and the available options of prenatal diagnosis. However, at age 16, life survival for the shunted group A (90%) is not significantly different than for the unshunted group B (83%), denoted by an asterisk in figure 3 ($p = 0.17$).

Figure 4 represents individuals alive at age 16, regardless of birth date. We compared survival of those who had CSF shunts in place (group A, n = 117) versus those who did not (group B, n = 56). Seventeen individuals without shunts and 5 individuals with shunts entered care after age 16, indicating that the vast majority of the outcomes

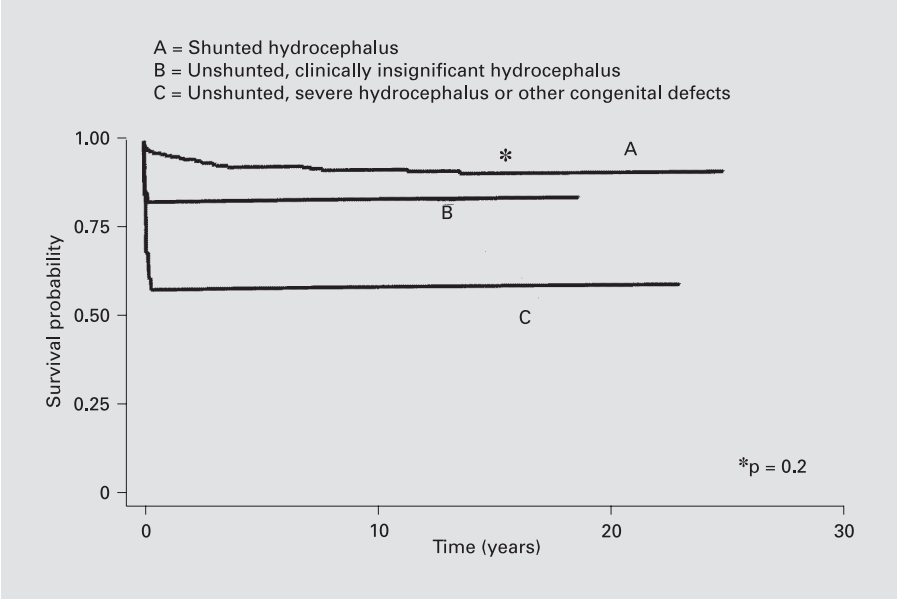

Fig. 3. Survival among patients born and treated after 1975 (n = 492). Group A (n = 401), group B (n = 56), group C (n = 35). Single time point analysis at age 16, marked by an asterisk, did not reveal statistical difference between groups A and B survival probability. The x-axis extends from birth to 24 years.

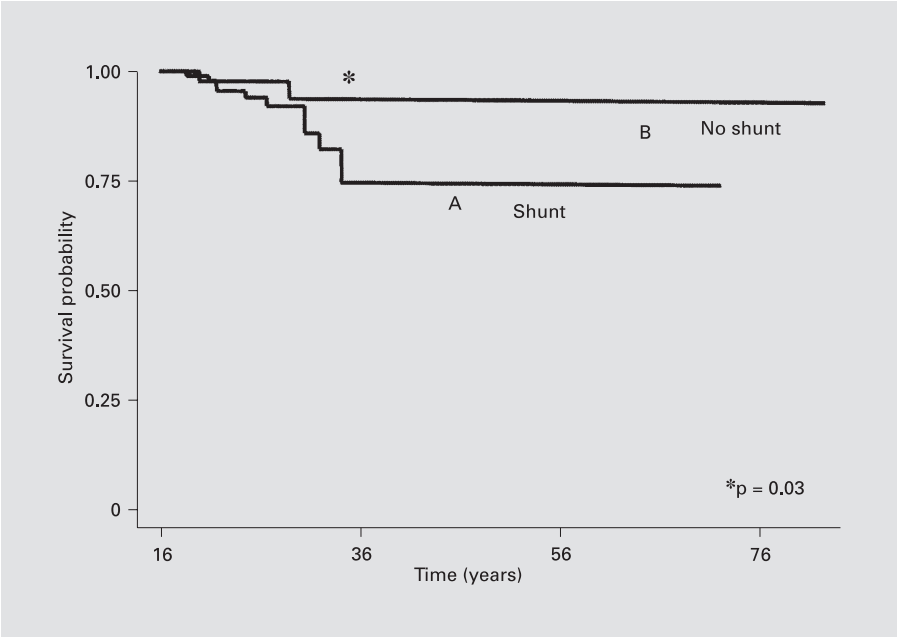

Fig. 4. Survival among all patients alive at age 16 categorized as group A (CSF shunt in place) or group B (no CSF shunt). There is a significant decrease in survival after age 35 in patients with shunts compared to those without, as marked by an asterisk. The x-axis extends from age 16 to 83 years.

reflected in the curves represent consistent care and access to medical technology from a single institution for both groups. Adults without CSF shunts had a survival probability of 94% at age 34 (n = 23). Individuals with shunts had a survival probability of 75% at age 34 years (n = 30). At age 42, there were less than 5 individuals in both groups, the power of the curves diminished, and results became unreliable. Despite the improved childhood survival of shunted individuals (born before 1975) and similar survival at age 16 regardless of shunt status (born after 1975), analysis revealed a decreased survival probability of almost 20% for individuals with shunted hydrocephalus versus unshunted hydrocephalus after age 35 (p = 0.03, 95% CI of the difference = 0.01–0.36 [11]).

Discussion

Over the years, studies have merged patient data for various neural tube defects when making survival predictions, including spinal defects with known increased longevity (i.e. meningocele, lipomeningocele) with those of decreased longevity (i.e. encephaloceles) [7, 13]. In this study, we developed survival probability for children born with MM and its associated sequelae: neurogenic bowel and bladder, paraparesis, Chiari II malformation, and hydrocephalus. Our data are consistent with a recent report from the United Kingdom, in which 117 patients with MM, born before the mid-seventies, were followed to adulthood. The authors estimated a median survival time of 30 years for individuals with MM [6].

A somewhat arbitrary year of 1975 was chosen to temporally reflect the vast changes in medical and surgical management of individuals with MM. The subsequent increase in patients treated after 1975 with CSF shunts may represent increased use of CSF shunts, decreased complications, change from invasive methods for evaluating brain fluid spaces to noninvasive methods, introduction of broad-spectrum antibiotics and newer shunt systems able to treat previously 'unshuntable' conditions [3, 5, 7, 15, 16]. This trend is consistent with other reports that conclude an improved prognosis may be possible for severely affected infants, if they are aggressively managed [2, 3, 15].

Prior to 1975, a larger proportion of patients were considered to have a very poor prognosis in our program. Infants in this category, in agreement with parental wishes, were offered nonsurgical supportive care with frequent follow-up. Of note, even without surgical intervention, a substantial proportion of these children survived infancy, contradicting a widely held belief that the initial birth examination could predict lethal birth defects with a high degree of certainty [17]. The number of individuals in our study receiving supportive care significantly diminished after 1975. The decrease is related to improved technology and the application of criteria set forth by Shurtleff et al. [5] in 1965, based on the observation that aggressive care (surgical and nonsurgical) may be more important in determining survival than selection at birth [3].

To better understand the relationship between shunted and unshunted individuals as they aged, we categorized all of our patients alive at age 16 into two groups, regardless of birth date. By 1975, even the older adults who had shunts placed years earlier should have been able to benefit from technological advances improving the prognosis of the younger cohort. We found that shunted adults had a decreased longevity after the age of 35 compared to their age-matched unshunted peers. Tomlison and Sugarman [18] reported 13 deaths from a cohort of 113 young adults with MM, of which 3 were from known complications, 4 died suddenly, and 2 adults developed increased intracranial pressure despite years of apparent 'shunt independence'. Subsequent studies have also demonstrated shunt-related mortality [19, 20]. Dunne et al. [21] described a significant problem for adults with MM in obtaining routine, knowledgeable health care. The absence of organized, multidisciplinary care for adults with significant congenital defects in our region may play a role in the morbidity and mortality seen in our patients [22].

Conclusions

Patients with MM treated after 1975 have a longer life expectancy than patients with MM treated between 1957 and 1974. The survival of patients with MM treated after 1975 is not associated with shunt status through 16 years of age. Individuals with MM, alive at 16 years of age, are at risk of decreased survival after age 34 if a shunt is in place. This study and other data describe potential long-term risks of shunted hydrocephalus. Further delineation of factors associated with shunted hydrocephalus leading to increased mortality need to be explored.

References

1 Stevenson RE, Allen WP, Pai GS: Decline in prevalence of neural tube defects in a high-risk region of the United States. Pediatrics 2000; 106:677–683.

2 Shurtleff DB, Lemire RJ: Epidemiology, etiologic factors, and prenatal diagnosis of open spinal dysraphism. Neurosurg Clin N Am 1998;6:183–193.

3 McLaughlin JF, Shurtleff DB, Lamers JY, et al: Influence of prognosis on decisions regarding the care of newborns with myelodysplasia. N Engl J Med 1985;312:589–594.

4 Leonard CO, Freeman JM: Spina bifida: A new disease. Pediatrics 1981;68:136–137.

5 Shurtleff DB, Hayden PW, Loeser JD, Kronmal RA: Myelodysplasia: Decision for death or disability. N Engl J Med 1974;291:1005–1011.

6 Hunt GM, Palmer C: The median survival time in open spina bifida. Dev Med Child Neurol 1997;39:568.

7 Mirzai H, Ersahin Y, Mutluer S, Kayahan A: Outcome of patients with myelomeningocele. Childs Nerv Syst 1998;14:120–123.

8 Steinbok P, Irvine B, Cochrane DD, Irwin BJ: Long-term outcome and complications of children born with myelomeningocele. Childs Nerv Syst 1992;8:92–96.

9 Laurence KM, Tew BJ: Natural history of spina bifida cystica and cranium bifidum cysticum. Major central nervous system malformations in South Wales. Arch Dis Child 1971;46: 127–138.

10 Shurtleff DB: Computer data bases for pediatric disabilities. Phys Med Rehabil Clin N Am 1991;2:665–687.

11 Newcombe RG: Interval estimation for the difference between independent proportions: Comparison of eleven methods. Stat Med 1998;17:873–890.

12 Shurtleff DB, Dunne K: Adults and adolescents with meningomyelocele; in Shurtleff DB (ed): Myelodysplasias and Exstrophies: Significance, Prevention, and Treatment. Orlando, Grane and Stratton, 1986, pp 433–448.

13 McDonnell GV, McCann JP: Issues of medical management in adults with spina bifida. Childs Nerv Syst 2000;16:222–227.

14 Freeman JM: The changing ethical issues in treatment of spina bifida: A personal odyssey. Ment Retard Dev Disabil Res Rev 1998;4: 302–307.

15 McLone DG: Results of treatment of children born with a myelomeningocele. Clin Neurosurg 1983;30:407–412.

16 Shurtleff DB, Kronmal R, Foltz EL: Follow-up comparison of hydrocephalus with and without myelomeningocele. J Neurosurg 1975;42: 61–68.

17 Lorber J: Results of treatment of myelomeningocele. An analysis of 524 unselected cases, with special reference to possible selection for treatment. Dev Med Child Neurol 1971;13: 279–303.

18 Tomlison P, Sugarman ID: Complications with shunts in adults with spina bifida. BMJ 1995;311:286–287.

19 Sgouros S, Maliuci C, Walsh AR, Hockley AD: Long-term complications of hydrocephalus. Pediatr Neurosurg 1995;23:127–132.

20 Tuli S, Drake J, Lamberti-Pasculli M: Long-term outcome of hydrocephalus management in myelomeningoceles. Childs Nerv Syst 2003; 19:286–291.

21 Dunne KB, Gingher N, Olsen LM, Shurtleff DB: Adults with spina bifida: A survey of their medical and social status; thesis, University of Washington, Seattle, 1986.

22 Kaufman BA, Terbrock A, Winters N, et al: Disbanding a multidisciplinary clinic: Effects on the health care of myelomeningocele patients. Pediatr Neurosurg 1994;21:36–44.