

Survival and mobility in open spina bifida: Comparison of results from the United States and the United Kingdom

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Abstract: The prognosis for survival in spina bifida is an important issue for life-care planners and care-givers. This study documents and compares long-term survival in open spina bifida in California, United States of America, and Cambridge, United Kingdom and investigates the relation between mobility in childhood and long-term survival. Survival after the age 6 years was similar in the two series, with a mortality rate of approximately 1% per year. Data from the California series showed that long-term survival was associated with gross motor function, specifically the ability to crawl or to stand without support. In the Cambridge cohort, mobility at mean age 9 years was a significant predictor of survival at the mean age of 35 years. We conclude that better gross motor function is associated with longer survival in open spina bifida.

Keywords: Survival, mortality, life expectancy, spina bifida, comparison, logistic regression, Kaplan-Meier, person-years, mobility, functional ability

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INTRODUCTION

Life expectancy is an important consideration in the planning of long-term care for persons with disabilities. This may be especially so in spina bifida, where almost all patients have physical, and often mental, disabilities.

The survival of infants with spina bifida has been examined previously in the scientific literature (1-9). One study followed a cohort of 479 children with spina bifida and hydrocephalus born during 1952-86 (2). In a subset of 255 children born from 1970-86, more than 30% died in the first year. After the age of 3 years, however, mortality rates dropped substantially. Other estimates of survival showed a similar pattern, with high mortality in the first two years and a gradual decline past age 3 years. In a study of infants with spina bifida born in the 1970s, only 57% survived the first year (1). Survival in the cohort was related to the type and level of the spinal defect, hydrocephalus, and presence of other birth defects. Survival has also been shown to be related to neurological level in terms of sensory level in infancy (5-10).

The neurological level of the spinal lesion affects the gross motor function (5). The relation is similar to that of spinal cord injury: those whose spinal malformation is higher on the spinal cord tend to have less

mobility. As mobility has been found to predict survival in spinal cord injury and cerebral palsy, both of which share similar features of disability with spina bifida, we examined the relation between survival and mobility, using mobility as a marker for sensory level and severity of disability (10-12).

METHODS

The California Department of Developmental Services (DDS), United States of America (USA) and the Cambridge Spina Bifida Cohort, United Kingdom (UK) were the two sources of data used for the study. The California data consist of 7,617 person-years from 1,041 spina bifida patients who received services from the DDS between January 1987 and December 2002. The DDS provides medical services, therapies, board and care, and respite services to all children in the State of California who have developmental disabilities.

The data were collected on the Client Development Evaluation Report (CDER) (13). This instrument contains over 200 psychological, medical, functional, behavioral, and cognitive items, and is completed approximately annually for all persons receiving services. Although the CDER lacks clinical information specific to spina bifida, limited information on bony

level (cervical, thoracic, or lumbo-sacral) and hydrocephalic status was available through the spina bifida ICD-9 code.

Spina bifida patients were identified by selecting the first CDER evaluation in the 1987-2002 study period with ICD-9 code 741 as the etiology of developmental disability. Although the database also contains persons with spina bifida occulta (ICD-9 756.17), these patients were excluded from the present study. Mortality information was obtained from California Department of Health Services, to which, by law, all deaths in California are reported.

The Cambridge cohort comprised 117 consecutive, unselected cases of open spina bifida born 1963-1970 at Addenbrooke's Hospital, Cambridge, UK, and has been described in detail elsewhere (5-7,14). In brief, the data for this cohort included detailed neurological and functional assessment starting at birth (14), with no loss to follow up and complete mortality information through April 2002. The cohort has been reviewed six times, in 1971, 1976, 1985, 1992, 1997, and 2002 (5,7,14). Deaths in this cohort were obtained through medical records and the Office of National Statistics.

Analytic methods

Survival analysis for the California patients was conducted using the pooled repeated observations method for analysis. In this method, the unit of observation is not a person, but a person-year. With each person-year we associated (1) a binary outcome variable indicating whether the person lived or died in that year, and (2) a set of explanatory variables. Logistic regression analysis was used to relate the outcome variable (lived/died) to the explanatory variables (15). This approach has been widely used in similar work (16-17). We modeled survival in the California data using a gross motor function scale based on the crawling and standing measure found on the CDER. We used three groups:

1. Those who cannot crawl, creep or scoot;
2. Those who can crawl, creep or scoot, but who cannot stand (even with minimal support); and
3. Those who can stand with minimal support or who have better functional abilities (e.g., can stand with no support, or who can walk).

We used logistic regression analysis to estimate the relative risks of these groups, other factors being equal. Based on this analysis, we estimated the mortality rates for persons in each age and mobility group. These rates

were then used to construct the survival curves for the three groups. The method is closely related to the standard proportional hazards model. Although the level of lesion and hydrocephalus has been identified in other studies as predictive of survival, we did not test these variables here as information was missing in many cases.

For comparison of survival between countries, we generated survival curves for the California and Cambridge cohorts. The California curve is based on age-specific annual mortality rates, calculated as the ratio of the observed number of deaths to the observed exposure time in each age group. Survival from age 3 years in the Cambridge series was calculated using the Kaplan-Meier survival function.

To model the relation between ambulation and survival in the Cambridge cohort, we used proportional hazards regression analysis for the 75 patients who survived and whose mobility was assessed at the mean age of 9 years.

RESULTS

Demographic characteristics are shown in tables 1 and 2. The 1,041 California patients had a mean age of 11

Table 1. Characteristics of the 7,617 person-years in the California series (n=1,041 persons)

Characteristic	Percent
Female	53
Crawling and Standing	
Does not crawl, creep or scoot	22
Crawls, creeps or scoots	34
Pulls to a standing position	6
Stands with support for at least 1 minute	17
Stands unsteadily alone for at least 1 minute	6
Stands well alone, balances well for at least 5 minutes	16

Table 2. Characteristics of the Cambridge cohort who survived to age 3 (n=83)

Characteristic	Percent
Female	59
Hydrocephalus	89
Ambulation at age 9* (n=75)	
Always uses wheelchair	13
Mostly uses wheelchair	36
Sometimes uses wheelchair	31
Walks independently	20

*When assessed at school at the mean age of 9 years

years at the start of the follow-up. In the Cambridge cohort, 83 (71%) of the 117 subjects survived to age 3 years and were included in the study. This group was followed prospectively to an average age of 35 years, with a maximum attained age of 38 years. About a fifth of each group had good mobility, being able to stand well alone and/or walk independently.

Comparison of survival between countries

Figure 1 compares survival from age 3 between the California and Cambridge series. Although survival in the UK cohort was lower initially, the curves are strikingly parallel thereafter. The UK cohort had a slightly better survival past age 30 years, ending at 61% versus the California survival of 53%. Although this comparison indicates that death rates after age 6 years were similar in the two series, it did not provide conclusive evidence for the similarity of these rates over time. It is possible that one or both study populations have experienced improvement in the mortality rates; we have not examined this possibility in the present study.

Survival is related to mobility

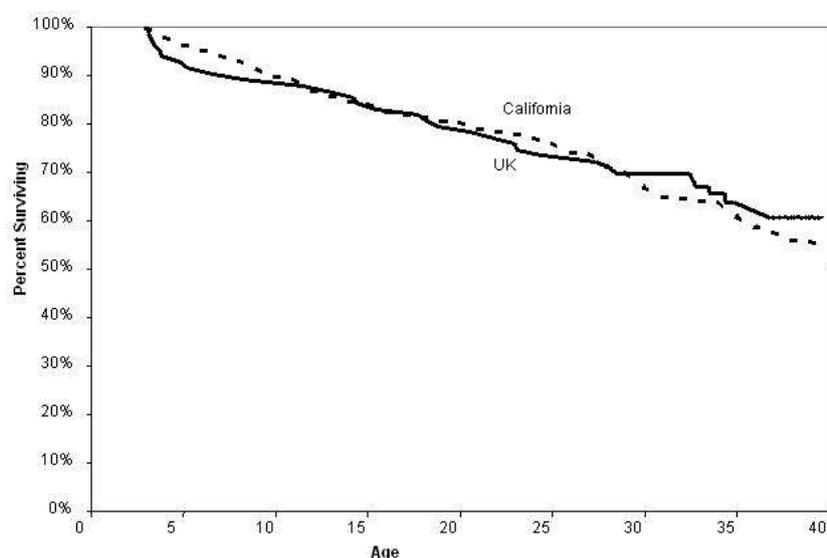
In both the California and Cambridge samples, survival into adulthood was significantly related to mobility in childhood. The model for the California data displayed in table 3 shows that those with better gross motor function have a significantly lower chance of dying in any given person-year. Those who cannot crawl have

six times the odds of death ($=1.00/0.15$), and those who can crawl but not stand well have twice times the odds of death ($=0.32/0.15$), compared with those who can stand with support or better. These odds ratios were then used to adjust the California survival curve given in figure 1, yielding the mobility-specific survival curves displayed as figure 2.

In the Cambridge cohort, survival into the third decade is significantly related to ambulatory ability at age 9 years. The model in table 4 shows that those who mostly or almost always used a wheelchair (when assessed at the mean age of 9 years) had 2.7 times the risk of dying as did those who walked or only occasionally used a wheelchair. Of these latter, 84% (32/38) survived to the mean age of 35, compared with 59% (22/37) of those who used a wheelchair mostly or always ($p < .05$).

Table 3. Survival is better in those with better mobility: Logistic regression model for the California data

Effect	Odds Ratio (95% CI)
Immobile	1.00 (reference group)
Crawls, creeps or scoots or pulls to stand	0.32 (0.21, 0.47)
Stands with support or better	0.15 (0.09, 1.38)



* By age 3 years, 29% (34/117) of the Cambridge Cohort had died.

Fig. 1: California vs UK Spina Bifida survival after age 3 years

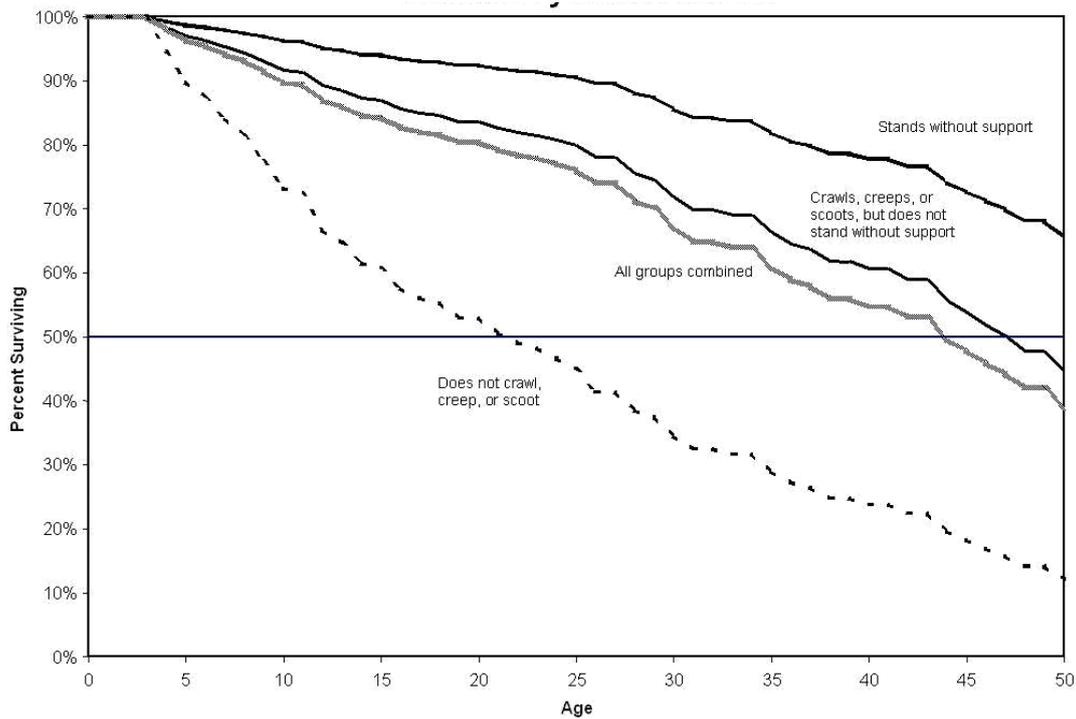


Fig. 2: Survival curves for California patients stratified by motor function

Table 4. Survival is better in those with better mobility: Cox proportional hazards model for the Cambridge cohort (n=75)

Effect	Deaths by mean age 35	Hazard Ratio (95% CI)
Mostly or almost always uses wheelchair at age 9 (n=37)	15	2.70 (1.02, 7.16)
Walks independently or sometimes uses wheelchair at age 9 (n=38)	6	

DISCUSSION

Our analyses confirm that survival in people with spina bifida past age 6 years is similar in the USA and UK, with a death rate of about 1% per year (18). The UK showed a higher death rate in the age range 3-6 years, as seen in the greater drop in survival in figure 1, but a lower death rate in the thirties. This difference may be because the UK experience for early childhood dates from the 1960s, two decades before the birth of most of

the cases in the California series. Advances in medicine since the 1960s, such as improved diagnosis and management of neurological and renal problems, may contribute to the mortality difference in early childhood.

The UK data have previously shown that neurological deficit in terms of sensory level in infancy predicts survival, hydrocephalus, IQ, visual defects, incontinence, and deaths from renal failure (5,7,14). In the absence of precise neurological information, however, the current study shows that long-term survival can, to some extent, be predicted by mobility. Mobility, an easily measured attribute related to disability, can be expressed either as crawling and standing, or as ambulation in childhood. This relation is useful for life-care planning as it can be easily and accurately assessed by persons with little or no clinical training.

Strengths and limitations

The strengths of this study are the large size of the California series (both in people and person-years), and the complete follow up and detailed assessment in infancy in the Cambridge cohort. The relatively large number of person-years from the California data

allowed us simultaneously to test the relation between age, functional abilities, and mortality in spina bifida. In this way, we could discern the overall relation of mobility in the data series while controlling for age. This in turn allowed for the mobility-adjusted survival curves presented in figure 2. The major strength of the Cambridge cohort is the detailed neurological assessment at birth and the complete follow-up across the life span.

The major weaknesses of the California data are incomplete clinical information on spina bifida and a lack of information from early childhood. This drawback makes comparison of survival in infancy between the US and UK data unfeasible. The weakness of the Cambridge data is the small size of the cohort. Whereas the complete follow-up removes the possibility of biases in survival estimates at young ages, the small size of the cohort makes the estimates of survival less precise.

Although we did not address the possibility of improvement in mortality rates over time for spina bifida, it is likely that improvement has occurred. A recent article based on a large population with cerebral palsy demonstrated a secular trend among severely disabled children and some adults with severe cerebral palsy (19). Again, as spina bifida shares common features with cerebral palsy, particularly in children under 6 years, it is likely that mortality rates for spina bifida have also improved.

Comparison with other studies

We are not aware of any other study that has related gross motor function to survival in spina bifida. Our findings are similar to results of mortality studies for persons with spinal cord injury, traumatic brain injury, and cerebral palsy (12,20), however. In each of these conditions, higher gross motor function is associated with better survival. Similarly, in spina bifida walking is related to severity of the lesion, and that those with more severe lesions have higher mortality has long been known (4,14,21).

Survival in the Cambridge cohort over the first year of life was similar to that in a cohort from the USA over the same period (1). In both groups, survival related to the level of the neurological deficit. Yet, no other studies have been conducted on survival in spina bifida up to the fourth decade. A recent study of 118 adults with spina bifida aged 20-25 years found 24% mortality but had 16% loss to follow-up (3). Additionally, an ongoing study of adolescents with spina bifida is in progress in the Netherlands (ASPINE), which includes

179 young adults aged 16-25 years (22). To the best of our knowledge, our study is the first comparison of long term survival in spina bifida between countries (10).

Implications

Long-term survival after the age of 6 years in open spina bifida is similar in the USA and the UK. This similarity may be because outcome depends mainly on the degree of neurological deficit at birth (1,20) and the benefits of treatment are limited (5). Another possible reason may be the propensity of adults with spina bifida to die of epileptic fits, pulmonary embolism, renal sepsis, or acute hydrocephalus without reaching hospital. Such events are unpredictable and largely unpreventable (6). As such, death rates for adults would be more difficult to improve than for children, where improvement in surgical techniques in the closure of lesions could have a dramatic impact on the rates of death by infection and complications.

We have presented evidence that long-term survival is related to mobility in childhood. Sensory level in infancy may be clinically more useful by providing additional information on continence and urological outcome (5,23). However, a simple functional gross mobility index such as the one used here would be easy for clinicians and laypersons alike to apply. Such an index therefore has the potential to be a useful tool for clinicians and caregivers when planning for the long-term needs of people with spina bifida.

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