Spinal Muscular Atrophy: Survival Pattern and Functional Status

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ABSTRACT. *Objective.* **Spinal muscular atrophy (SMA) is common. The prevalence of SMA in southern Chinese is 1 in 53 000. The clinical course is variable. The traditional classification of SMA includes age of onset, age of death, achievement of motor milestones, and ambulatory status as criteria. There was a lack of inclusion of the best lifetime functional status of any child with SMA. With the advances in medical care, the life expectancy and ambulatory status of patients with SMA have improved. The objective of this study was to assess the survival pattern, ambulatory status, and functional status of children with SMA.**

Methods. **Patients with SMA were recruited from the neuromuscular clinic of the Duchess of Kent Children's Hospital, which is a university-affiliated hospital, and the Families of SMA in Hong Kong. By September 2002, 102 SMA cases had been registered in the Duchess of Kent Children's Hospital neuromuscular clinic and Families of SMA registry, and 83 patients were analyzed. Among them, 39 were recruited for the administration of Functional Independence Measure for Children (WeeFIM), an assessment tool for functional status that has been previously validated by us for Chinese children. The diagnosis of SMA was made from clinical history, serum muscle enzyme, electromyography, muscle biopsy, and, recently, by molecular studies. In Hong Kong, molecular tests of the survivor motor neuron gene was available since 1995. A total of 36 in our cohort of 83 patients had the diagnosis confirmed with molecular analyses. We adopted the classification of SMA from previous studies in which the criteria were based on the International SMA consortium (1992) with modifications according to the 59th European Neuromuscular Center International Workshops. As only SMA patients with childhood onset were studied, we did not include any type IV patients in our study. Parents were interviewed and records were reviewed for demographic and clinical data, including age of onset, gender, family history, motor milestones, disease progression, loss of motor function, and involvement of respiratory or bulbar muscles. We define the age of disease onset as the age in which the first abnormalities were obvious from the medical records or from the descriptions of the parents about the first signs of weakness, eg, age of achievement of certain motor milestones or loss of functions. For the ambulatory status, we define "being ambulatory" as having the ability to walk for 100 meters, either with assistance such as calipers or walkers or without assistance. Actuarial survival curves were obtained by using the Kaplan-Meier method for calculating survival probabilities and probabilities of remaining ambulatory. The parents or the chief caregivers were interviewed for functional status using WeeFIM at the last registered date in September 2002. The WeeFIM consists of 3 domains: 1) self-care, 2) mobility, and 3) cognition. The self-care domain consists of 8 items, namely eating, grooming, bathing, dressing (upper body), dressing (lower body), toileting, and bladder and bowel management. The mobility domain consists of 5 items: transfer from chair or wheelchair, transfer to toilet, transfer to tub or shower, walking/wheelchair/crawling distance, and moving up and down stairs. The cognition domain assesses comprehension, expression, social interaction, problem solving, and memory. A scoring scale from 1 to 7 was used (1 = total assistance, 2 = maximal assistance, 3 = moderate assistance, 4 = minimal contact assistance, 5 = supervision, 6 = modified independence, and 7 = complete independence). The maximum total WeeFIM score is 126, and the maximum score for self-care, mobility, and cognition are 56, 35, and 35, respectively.**

Results. **For type I SMA (n = 22), the survival probabilities at 1, 2, 4, 10, and 20 years were 50%, 40%, 30%, 30%, and 30%, respectively. For type II SMA (n = 26), the survival probabilities at 1, 2, 4, 10, and 20 years were 100%, 100%, 100%, 92%, and 92%, respectively. Sixteen of the SMA I patients and 4 of the SMA II patients died of cardiorespiratory failure. The 5 surviving SMA I patients all were ventilator dependent. All SMA III patients were surviving at the time of study. The probability of remaining ambulatory at 2, 4, 10, and 20 years after onset was 100%, 100%, 81%, and 50% for type IIIa (age of onset <3 years) and 100%, 100%, 84%, and 68% for type IIIb (age of onset between 3 and 30 years), respectively. The interval between disease onset and inability to walk was 15.0 ± 10.9 years (mean ± standard deviation) and 21.2 ± 11.7 years for patients with SMA IIIa and IIIb, respectively. Only 39 patients participated in the WeeFIM interview as 20 had already died at the time of study and 24 refused participation. No difference could be found in the age of onset, gender, or types of SMA between those who participated (n = 39) and those who did not (n = 24). The mean total WeeFIM quotients were 24% for SMA type 1, 57% for SMA type 11, 75% for SMA type IIIa, and 78% for SMA type IIIb. For the self-care domain, 100% SMA type I and 73% SMA type II patients required assistance, whereas 55% and 63% of SMA types IIIa and IIIb patients achieved functional independence. Bathing and dressing (upper and lower body) were items with which most SMA children required help or supervision. For the mobility domain, assistance was needed in >90% of**

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SMA types I, II, and IIIa and in 63% of SMA type IIIb patients. Stair management was the major obstacle for independence in achieving mobility for all types of SMA. For the cognition domain, performance was the best among the 3 domains, and 60% of SMA type II, 78% of SMA type IIIa, and 90% of SMA type IIIb patients achieved functional independence. However, except for SMA type IIIb, a significant proportion of patients still need assistance or supervision in the area of problem solving. Statistically significant differences were found in the WeeFIM scores between type I and type II and between type IIIa and IIIb patients. However, no significant difference could be observed between type II and type IIIa SMA patients in the overall WeeFIM scores or performance in any of the 3 domains.

Conclusion. **We found that there was improvement in survival in SMA patients as compared with other studies. Assistance or supervision was needed for the majority of SMA patients for both mobility and self-care domains. With improvement in survival as a result of medical advances, assessment of the most current or the best-ever functional status at a designated age might be an important criterion for classification of SMA.** ***Pediatrics*** **2004; 114:e548–e553. URL: www.pediatrics.org/cgi/doi/10.1542/peds.2004-0668;** ***spinal muscular atrophy, Functional Independence Measure for Children, Chinese children.***

ABBREVIATIONS. SMA, spinal muscular atrophy; ENMC, European Neuromuscular Center; DKCH, Duchess of Kent Children's Hospital; FSMA, Families of SMA; WeeFIM, Functional Independence Measure for Children.

Spinal muscular atrophy (SMA) is a common neuromuscular disease. The incidence of SMA is estimated to be 1 in 10 000. The prevalence is much lower as high mortality is associated with its severe form, type I SMA. Despite establishment of SMA registries in various ethnic groups, there is still lack of epidemiologic data of SMA in Chinese. In our recent study in 2001, the prevalence of SMA was estimated to be 1 in 53 000 in southern Chinese.[1]

Although classified into 3 subtypes, the clinical course is highly variable, and it is more of a continuous spectrum with age of onset from birth to adulthood; age of death spanning from early infancy to adulthood; and even variable tempo of progression, depending on the respiratory function and the availability of ventilator support.[2,3] Thus, additional modifications had been suggested after the initial classification developed in the International SMA Consortium in 1992.[4] In 1999, a major revision was adopted by the European Neuromuscular Center (ENMC), in which achievement of motor milestones was included as an important criterion in the classification.[5]

Studies had been focused mainly on the life expectancy and ambulatory status, with less emphasis on the level of functional achievement. With advances in medical care, such as effective antibiotics for recurrent pneumonia and ventilatory support for respiratory failure, there is now a higher chance of survival. Moreover, the overall functional and rehabilitative aspects of SMA children has also been improved over the past decades. According to the World Health Organization proposal of the International Classification of Impairments, Disabilities, and Handicaps,[6] the concept of "burden of care," ie, the type and amount of assistance that a child with a certain disability requires for performing basic life activities effectively, should be measured for disabled children for better resource allocation, rehabilitation service planning, and education. Our objective is to study the survival pattern and functional status of SMA children in Hong Kong.

METHODS

Case Ascertainment

A neuromuscular clinic was established in 1984 in the Duchess of Kent Children's Hospital (DKCH), a university-affiliated hospital equipped with both diagnostic and rehabilitative facilities for children with various neurologic disorders. SMA is the second most common inherited neuromuscular disease in our database collected for Chinese children.[1] The Families of SMA (FSMA) was founded in Hong Kong in 2000[5,7] with the objectives of promoting public awareness, providing financial support to needy patients and families, and establishing a central registry of SMA patients in Hong Kong. By September 2002, 102 SMA patients had been registered in the DKCH neuromuscular clinic and FSMA registry, and 83 patients with available clinical information were analyzed for the survival pattern. Among them, 39 active patients were recruited for the administration of Functional Independence Measure for Children (WeeFIM) with informed consent.

SMA Classification

There has been controversy as to the exact criteria of classification of SMA.[2,3] In 1992, the International SMA Consortium adopted defined ages of onset and death as classification criteria[8]:

1. SMA type I (severe): onset from birth to 6 months; patients are never able to sit without support, and death occurs usually at 2 years
2. SMA type II (intermediate): onset before 18 months; patients are able to sit but are unable to stand or walk unaided, and death occurs usually at older than 2 years of age
3. SMA type III (mild): onset after 18 months of age; patients are able to stand and walk, and death occurs in adulthood.

In this study, we adopted the criteria of Zerres and the 59th ENMC international Workshops.[4] The modification in definition includes

1. Type I SMA patients can never sit alone.
2. Type II SMA patients can sit alone but can never walk.
3. Type III SMA patients can walk without support. Type IIIa has age of onset <3 years, and IIIb has age of onset 3 to 30 years.
4. Type IV SMA patients have age of onset >30 years.

As we studied only SMA patients with childhood onset, no type IV patients were included in our study.

Clinical Data and Natural History

All medical records were reviewed. The diagnosis of SMA was made from clinical history, serum muscle enzyme, electromyography, muscle biopsy, and, recently, molecular studies. In Hong Kong, molecular test of the survivor motor neuron gene was initially available as a research protocol in our university in the period from 1995 to 1997.[9,10] Since 1997, this service has been available in the government genetic unit under the Department of Health. A total of 37 patients in our cohort of 83 patients had their diagnosis confirmed with molecular analyses.

Parents were interviewed for demographic and clinical data, including age of onset, gender, family history, motor milestones, disease progression, loss of function, respiratory involvement, and bulbar involvement. The age of disease onset was defined as the age at which the first abnormalities were obvious from the medical records or from the descriptions of the parents about the first signs of weakness, eg, age of motor milestones or loss of functions. As there might be recall bias for such a chronic disorder, we tried to get most information concerning age of onset from the medical

TABLE 1. Characteristics of SMA in Hong Kong ($N = 83$)

SMA Type	*n*	Gender, M:F	Mean Age of Onset ± SD, mo	Deceased	Nonambulatory	Ambulatory
I	22	9:13	1.6 ± 2.1	16	6	0
II	26	9:17	11.5 ± 7.0	4	22	0
IIIa	16	9:7	15.7 ± 7.4	0	10	6
IIIb	19	7:12	83.1 ± 96.3	0	6	13

TABLE 2. Survival Probability in SMA Types I, II, and III

SMA Type	Age in Years, %					
	1	2	4	10	20	40
I	50	40	30	30	30	—
II	100	100	100	92	92	88
IIIa	100	100	100	100	100	100
IIIb	100	100	100	100	100	100

records as the "age of onset" has always been meticulously found out for classification and prognostication.

We define "being ambulatory" as having the ability to walk with (calipers or walkers) or without assistance for 100 meters. Actuarial survival curves were obtained by using the Kaplan-Meier method for calculating survival probabilities and probabilities of remaining ambulatory.

Administration of WeeFIM

WeeFIM was developed for rehabilitative aspects of patients with disabilities and was based on the conceptual framework of "pathology, impairment, disability, and handicap" and the "burden of care" by the World Health Organization. It has been used in children with various acute and chronic neurodevelopmental disorders,[11,12] and its Chinese version has been validated.[13,14]

The parents or the chief caregivers were interviewed by a trained research assistant (S.H.) for WeeFIM scoring in September 2002. WeeFIM consisted of 3 main domains: 1) self-care, 2) mobility, and 3) cognition. The self-care domain consists of 8 items: eating, grooming, bathing, dressing (upper body), dressing (lower body), toileting, and bladder and bowel management. The mobility domain consists of 5 items: transfer from chair or wheelchair, transfer to toilet, transfer to tub or shower, walking/wheelchair/crawling distance, and moving up and down stairs. The cognition domain assesses the child in terms of comprehension, expression, social interaction, problem solving, and memory.

A scoring scale from 1 to 7 was used (1 = total assistance, 2 = maximal assistance, 3 = moderate assistance, 4 = minimal contact assistance, 5 = supervision, 6 = modified independence, and 7 = complete independence). The score was categorized into 1) requiring help or assistance (score 1–4), 2) requiring supervision (score 5), and 3) requiring no help (score 6–7). The maximum total score is 126, whereas the maximum scores for self-care, mobility, and cognition are 56, 35, and 35, respectively.

Statistical Analysis

Unpaired *t* test was used to determine any difference in the overall WeeFIM scores or in the 3 domains between the different types of SMA patients. $P < .05$ is considered statistically significant.

Results

Survival Pattern

The gender, age of onset, classification, and status of the 83 SMA patients are summarized in Table 1. Seventy-nine of them were Chinese.

Seventy-two percent (16 of 22) of the SMA I patients and 15% (4 of 26) of SMA II patients have died. The cause of death was cardiorespiratory failure for all of them. The 5 surviving SMA I patients (aged 8–35 years) were all ventilator dependent, with 1 on nocturnal continuous positive airway pressure and 4 on intermittent positive pressure ventilator via tracheostomies. These 4 patients have been assessed with standardized intelligence tests, and all had normal intelligence.

All SMA III patients were surviving at the time of study. The survival probabilities of patients with types I to III are listed in Table 2 and expressed as a survival curve in Fig 1 by Kaplan-Meier method. The probabilities of retaining the ability to walk with assistance for 100 meters from disease onset up to 40 years for SMA III patients are summarized in Table 3 and Fig 2. The interval between disease onset and inability to walk was 15.0 ± 10.9 years (mean ± SD) and 21.2 ± 11.7 years for patients with SMA IIIa and IIIb, respectively.

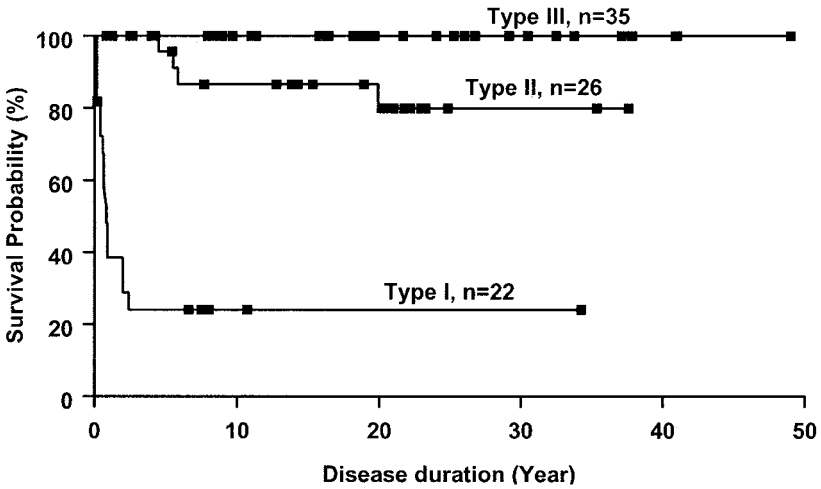

Fig 1. Kaplan-Meier survival curves for SMA I, II, III.

TABLE 3. Probability of Remaining Ambulatory After Onset in SMA Types IIIa and IIIb

SMA Type	Age in Years, %					
	1	2	4	10	20	40
IIIa	—	100	100	75	50	38
IIIb	—	100	95	79	68	68

TABLE 4. Comparison of SMA Patients Who Did and Did Not Participate in the WeeFIM Interview

Demographics	WeeFIM Done (N = 39)	WeeFIM Not Done (N = 24)	P Value
Gender			
Male	19	10	.586 (χ^2 test)
Female	20	14	
Age of onset, mo			
Mean	36.38	28.63	.632 (unpaired t test)
SD	72.97	38.15	
Median	15	12.5	
SMA type			
I	4	2	
II	15	7	.799 (χ^2 test)
IIIa	9	8	
IIIb	11	7	

Functional Status by WeeFIM Scores

Thirty-nine patients (and parents) participated in the WeeFIM interview. Those who did not participate had died (n = 20) by September 2002. Twenty-four parents did not consent for WeeFIM evaluation. For those who died were 16 SMA I and 4 SMA II. Table 4 showed the comparison between groups who participated or did not participate in the WeeFIM interview, excluding the deceased cases. No difference could be found in their age of onset, gender, or types of SMA.

Mean total scores (mean total quotient) were 30 (24%) of 126, 72 (57%) of 126, 94 (75%) of 126, and 97 (78%) of 126 for types I, II, IIIa, and IIIb, respectively. The WeeFIM profiles for different items in the domains of self-care, mobility, and cognition are illustrated in Fig 3, and the mean scores are calculated in Table 5.

Self-Care Domain

All type I and 73% of type II patients required assistance, while 55% and 63% of IIIa and IIIb patients achieved functional independence. Bathing and dressing (upper and lower body) were items with which most patients required help or supervision.

Mobility Domain

Assistance was needed in >90% of patients with SMA types I, II, and IIIa and in 63% with type IIIb. Stair management was the major obstacle for independence in mobility for SMA patients of all 3 types.

Cognition Domain

Performance in the cognition domain was the best among the 3 domains, and 60% of SMA II, 78% of SMA IIIa, and 90% of SMA IIIb patients had achieved functional independence. However, except for SMA IIIb, a significant proportion of patients would need assistance or supervision in the area of problem solving.

There was a statistically significant difference in the total WeeFIM scores between type I and type II SMA ($P < .001$) and between type IIIa and type IIIb SMA patients ($P < .009$). However, no significant difference could be observed between type II and type IIIa patients in their overall performance ($P = .456$) and performance in all 3 individual domains.

DISCUSSION

Our cohort of 83 SMA patients is representative of the SMA profile in Hong Kong as our cases were recruited through FSMA and DKCH, which were the only self-help group for SMA patients and the only medical center providing comprehensive neuromuscular rehabilitative services in Hong Kong.

Survival Pattern of SMA

Only 2 studies of the natural history of SMA patients were available[4,15] from literature. Zerres and colleagues reported 445 and 569 SMA cases in these studies published in 1995 and 1997, respectively. The survival probabilities at 2, 4, 10, and 20 years were 32%, 18%, 8%, and 0%, respectively, in SMA I patients and 100%, 100%, 98%, and 77%, respectively, for type II patients. Better survival is observed in our SMA patients, especially in those with type I. This difference became more marked as the survival time

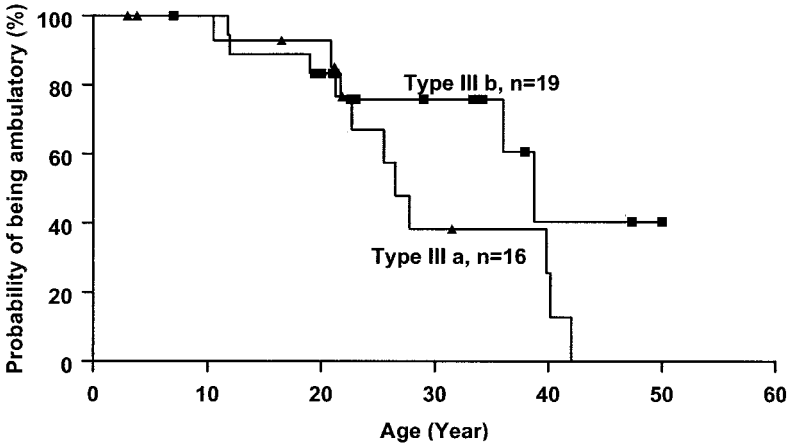

Fig 2. Probability of SMA III patients' being ambulatory after disease onset.

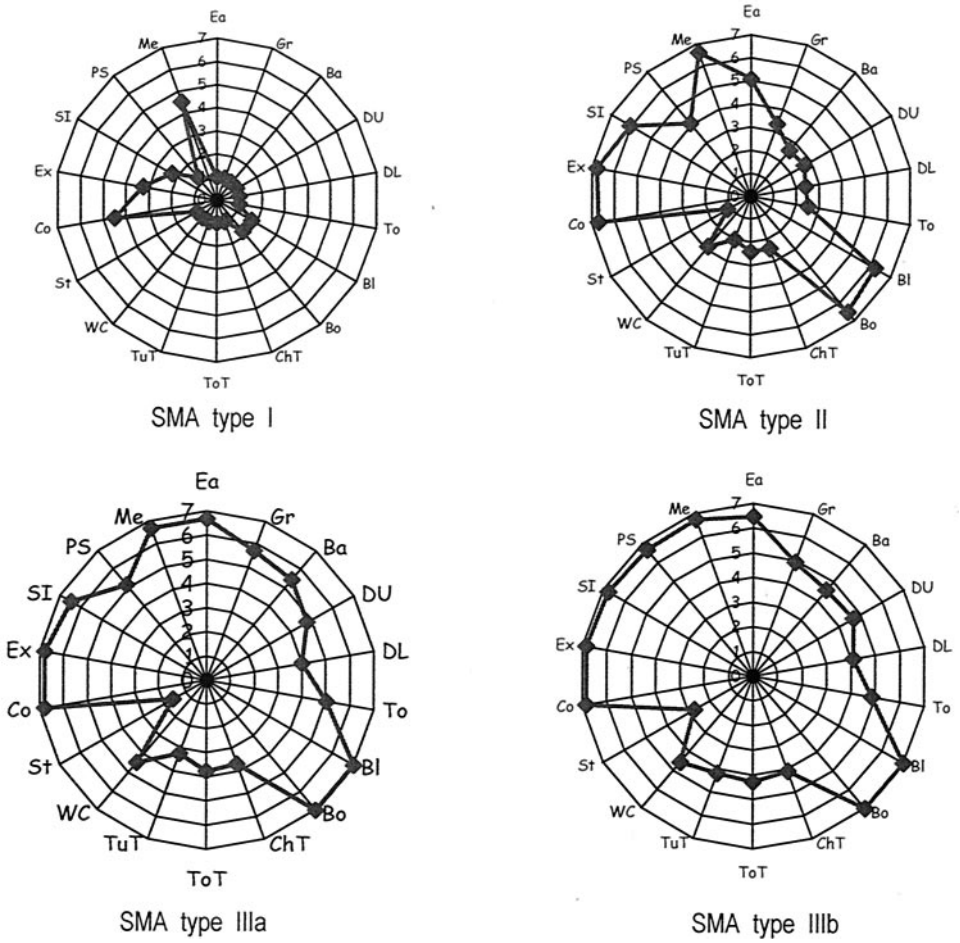

Fig 3. WeeFIM profile of patients with SMA I (n = 4), II (n = 15), IIIa (n = 9), and IIIb (n = 11). Ea, eating; Gr, grooming; DU, dressing (upper); DL, dressing (lower); Bl, bladder; Bo, bowel; ChT, bed/chair/wheelchair transfer; ToT, toilet transfer; TuT, tub/shower transfer; WC, walk/wheelchair; ST, stairs; Co, comprehension; Ex, expression; SI, social interaction; PS, problem solving; Me, memory.

TABLE 5. Mean WeeFIM Scores ±SD in SMA Patients

Domains	Maximum Score	SMA I	SMA II	SMA IIIa	SMA IIIb	*P* Values
Self-care	56	9.5 ± 1.9	31.3 ± 11.1	45.6 ± 10.1	43.5 ± 14.1	I vs II, <.001*; II vs IIIa, .325; IIIa vs IIIb, .014*
Mobility	35	5.0 ± 0.0	10.8 ± 7.0	16.7 ± 5.6	18.2 ± 12.1	I vs II, <.001*; II vs IIIa, .555; IIIa vs IIIb, .003*
Cognition	35	15.8 ± 8.0	29.4 ± 4.6	31.8 ± 4.6	33.73 ± 3.3	I vs II, .006*; II vs IIIa, .258; IIIa vs IIIb, .715
Total	126	30.3 ± 8.4	72.2 ± 19.0	94.0 ± 16.1	97.0 ± 24.2	I vs II, <.001*; II vs IIIa, .456; IIIa vs IIIb, .009*

* Statistically significant difference.

was extended. One SMA type 1 male patient in our cohort survived at 35 years, and his respiratory function was stable despite being bedridden since birth. In our series, 5 of the 6 surviving SMA I patients were dependent on ventilatory support, whereas no information was provided by Zerres in the 2 studies for comparison. However, we still postulate this as a major reason for the improvement in survival as this has been the major change in the management of SMA patients in these 5 to 10 years.

For our type III patients, their life expectancies are similar to the normal population at least up to 40 years of age. None of our patients with type III SMA died. Zerres reported that the prognosis differed for those with onset before or after 3 years of age in terms of the probability of remaining ambulatory.[14] Similar observations were made in our cohort. Subdivision of type III SMA seems justified as there is a 6-year difference in the duration of remaining ambulatory from disease onset when comparing SMA IIIa and IIIb patients (Table 3, Fig 2).

Functional Status

Mobility and Self-Care Domain

The dependence on self-care and mobility observed was obviously related to the disease nature itself. Assistance was necessary in most aspects of the mobility domain in all types of SMA, and >70% of type I and II patients required assistance.

Cognition Domain

A previous study[16] showed that children with SMA had general intelligence in the normal range, and then by adolescence, the environmentally mediated aspects of intelligence were higher in patients with SMA than normal control subjects. This was speculated to be compensating the restrictions as a result of their physical disability. It is worth noting that the methods of assessment used were various intelligence tests without a motor component or a time limit required. Our assessment of cognition by WeeFIM emphasized the evaluation of the real-life performance in daily activities. Functional independence could be achieved in most items in the cognition domain by our patients. However, assistance or supervision would still be necessary in problem solving in the daily activities in our SMA patients.

It must be pointed out that WeeFIM is an assessment for the functional independence standardized for normal children 6 months to 6 years of age. Therefore, there is a possible ceiling effect in assessing patients with mental age above 6 years. Other specialized forms of intellectual assessment should be performed when the purpose is beyond functional assessment, eg, when assessing the educational needs of these patients.

Implication of the Study

There are inadequacies in the classification of SMA with strict definition of ages of onset and death being emphasized. It has long been known that there are "long-term" survivors who did not comply with the classification criteria by age of onset or age of death. Furthermore, the classification did not predict the duration of preserved motor functions, eg, ability to sit and ability to walk. These limitations persist even in the revised ENMC classification, of which more emphasis was put on the attainment of motor milestones and the motor function. There is still inadequate reflection in the existing classification on the functional status of SMA patients who could have better overall survival with advancement of medical care.

We had reported the survival pattern and functional status of patients with SMA in Hong Kong. From historical comparison, there seemed to be an improvement in the survival probability of these patients even in the most severe type. This could be attributed to the advances in medical care, especially in pulmonary rehabilitation and ventilatory support. Functional assessment, by WeeFIM scoring, is effective in identifying areas in activities of daily living that need extra assistance or supervision, eg, self-care, mobility, and problem solving. The current classification of SMA, emphasized on the age of onset, motor developmental milestones, and age of death, did not address the functional status of SMA patients. With the encouragement from improved survival in our SMA patients, we recommend incorporating functional assessment into the classification of SMA in the future for prognostication.

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REFERENCES

1. Chung B, Wong V, Ip P. Prevalence of neuromuscular diseases in Chinese children: a study in southern China. *J Child Neurol.* 2003;18: 217–219
2. Dubowitz V. Chaos in classification of the spinal muscular atrophies. *Neuromuscul Disord.* 1991;1:77–80
3. Dubowitz V. Chaos in classification of the spinal muscular atrophies: a possible resolution. *Neuromuscul Disord.* 1995;5:3–5
4. Zerres K, Rudnik-Schoneborn S. Natural history in proximal spinal muscular atrophy—clinical analysis of 445 patients and suggestions for a modification of existing classifications. *Arch Neurol.* 1995;52:518–523
5. Zerres K, Davies KE. Workshop Report. 59th ENMC International Workshop: Spinal muscular atrophies: recent progress and revised diagnostic criteria. *Neuromuscul Disord.* 1999;9:272–278
6. *International Classification of Impairments, Disabilities, and Handicaps: A Manual of Classification Relating to the Consequences of Diseases*. Geneva, Switzerland: World Health Organization; 1980
7. Website of FSMA Charitable Trust. Available at: www.fsma.org
8. Munsat TL, Davies KS. International SMA consortium meeting (26–28 June 92, Bonn, Germany). *Neuromuscul Disord.* 1992;2:423–428
9. Wong V, Chan V. Molecular genetic study of childhood form of spinal muscular atrophy (SMA). *J Child Neurol.* 2001;16:291–294
10. Chan V, Yip B, Yam I, et al. Carrier incidence for spinal muscular atrophy in southern Chinese. *J Neurol.* 2004, in press
11. Msall ME, Di Gaudio KM, Roberts BT. The Functional Independence Measure for Children (WeeFIM): conceptual basis and pilot use in children with developmental disabilities. *Clin Pediatr.* 1994;33:421–430
12. Leonard S, Msall M, Bower C, Tremont M, Leonard H. Functional status of school-aged children with Down syndrome. *J Paediatr Child Health.* 2002;38:160–165
13. Wong V, Wong S, Chan K, Wong W. Functional Independence Measure (WeeFIM) for Chinese children: Hong Kong cohort. *Pediatrics.* 2002; 109(2). Available at: www.pediatrics.org/cgi/content/full/109/2/e36
14. Yung A, Wong V, Nursing Team. Outcome measure for paediatric rehabilitation: use of Functional Independence Measure for Children (WeeFIM). A pilot study in Chinese children with neurodevelopmental disabilities. *Pediatr Rehabil.* 1999;1:21–28
15. Zerres K, Rudnik-Schoneborn S, Forrext E, et al. A collaborative study on the natural history of childhood and juvenile onset proximal spinal muscular atrophy (type II and III SMA): 569 patients. *J Neurol Sci.* 1997;146:67–72
16. Von Gontard A, Zerres K, Backes M, et al. Intelligence and cognitive functions in children and adolescents with spinal muscular atrophy. *Neuromuscul Disord.* 2002;12:130–136

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