Derivation of an Ambulatory Prognostic Score Chart for Thai Children with Cerebral Palsy Aged 2 to 18

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Background: *Most parents want to know that their children with cerebral palsy will be able to walk. A simple tool to predict ambulatory status and one uses The Gross Motor Function Classification System is still lacking.*
Objective: *To develop a simple prognostic score chart for predicting ambulatory status in Thai children with cerebral palsy.*
Material and Method: *Four hundred seventy one children with cerebral palsy aged 2 to 18 registered and treated at six special schools or hospitals for children with physical disability between 2008 and 2013 were recruited. Baseline characteristics and clinical histories of children with cerebral palsy were collected from medical and physical therapy records. Ambulatory status was classified as three ordinal scales by The Gross Motor Function Classification System - Expanded and Revised version.*
Results: *Multivariable ordinal continuation ratio logistic regression analysis identified age, type of cerebral palsy, sitting independently at the age of two, and eating independently as significant predictors of ambulation. These items were combined into a clinical prediction score: non-ambulation (scores <7), assisted ambulation (scores 7 to 8), and independent ambulation (scores >8).*
Conclusion: *The prognostic tool has high discriminative values of ambulatory status among children with cerebral palsy. However, the validation of this tool needs to be tested in other subjects before clinical practice application.*

Keywords: *Cerebral palsy, Clinical prediction rule, Decision support techniques, Prognosis, Walking*

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Cerebral palsy (CP) is a disorder of motor control as a result of damage to the developing brain[1]. In developed countries, over the last three decades, the probability of survival has increased even in children with severe disabilities. In contrast, the prevalence of CP has not decreased but remained constant as about 2 to 3 per 1,000 live births[2]. Thailand has never had a true study on the prevalence of CP because there is no database or Cerebral Palsy Registry. There is only reported Disability Survey by the National Statistical Office, showed that among the 29,841 persons with CP, the most (12,019) were located in the northeastern part of the country, followed by the remaining (8,944) in northern Thailand[3].

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When children are first diagnosed as being CP, most parents ask the following questions: 'Will my child walk?' and 'When will he/she walk?'. The prognosis for their ambulation is very difficult because of several factors can influence the ambulatory status of a child during his/her growth. Nonetheless, the identification of predictors for ambulation is most important in order to assist in formulating an appropriate plan of intervention[4-6]. This is important for prognostic capacity regard to walking tends to be poor, an appropriate treatment planning is the most effective way to prevent the loss of ambulatory capacity[7].

The scoring method for the prognosis for walking in children with CP has been previously established by Bleck in 1975[8]. This scoring system has seven primitive reflexes and postural reactions as predictors, while there have also been other clinical predictors affecting walking prognosis[4,5,9-13]. This scoring method was discriminated into good prognosis, guarded prognosis, and poor prognosis. He stated that

it appeared simple, easy to understand, and easy to apply. It may be inappropriate to use in some context; however, a recent correlational study in Japan[14] showed that there was no difference in Bleck's scores between the ambulation group and the non-ambulation group. A large retrospective study conducted by Wu et al[5] created a simple tool for predicting the probability of ambulatory outcome from various levels in children with CP aged 2 to 14. This tool was divided into four ambulatory charts according to gross motor function achieved at the age of two, using Aalen-Johansen estimators of long-term transition probabilities. Additionally, there were also prognostic tools of gross motor function[15,16]. The gross motor function curves among the 5-level The Gross Motor Function Classification System (GMFCS) were constructed to inform regarding the prognosis of children with CP at each age.

Performing a comparison between the different studies is difficult because of the variations in the definitions of ambulatory operational[17]. In 1997, Palisano et al[18] created a five-level of GMFCS for children with CP and edited it in 2007[19]. Only the studies, recently, of Simard-Tremblay et al[12] and Kułak et al[13] used the GMFCS as a tool to classify ambulation. Many experts in clinical practice have developed their own specific criteria for predicting the ambulatory status in these children. These criteria may provide reasonable prognostic accuracy, but they are not necessarily transferable to and applicable in other contexts[4]. Although the prognostic tools for gross motor function of children with CP have been developed[5,8,15,16], a simple tool to predict ambulatory status and one that uses GMFCS is still lacking. Therefore, the study aims to develop a simple prognostic score chart for predicting the ambulatory status in Thai children with CP from the authors' prognostic predictors[20].

Material and Method

Ethics approval

The present study was approved by the Ethics Committee of the Faculty of Medicine, Chiang Mai University (The IRB approval number 188/2013), and Rajanagarindra Institute of Child Development, Chiang Mai. The participants were informed of the purpose and procedures of the present research. All the participants or their parents signed a written informed consent to participate in the study.

Study design and data collection

The medical and physical therapy records of children with CP were retrospectively reviewed between 2008 and 2013. They were registered and treated at six special schools or hospitals for children with physical disability in northeastern and northern Thailand. They were recruited if aged 2 to 18 and have been diagnosed by physicians or physiotherapists. The following criteria were the reasons for exclusion from the study: the children being duplicated between settings, not meeting the inclusion criteria, being diagnosed after two years old, unable to contact the parents or caregivers, death, and declining to participate.

Outcome variable

The GMFCS was used to describe walking ability. This tool had five ordinal levels: I) walks without limitations, II) walks with limitations, III) walks using a hand-held mobility device, IV) self-mobility with limitations or may use powered mobility, and V) transported in a manual wheelchair[19]. The subjects were assessed using the GMFCS - Expanded and Revised family and self-report questionnaires, which have been allowed to be translated into Thai language[21]. We classified the ambulatory status as three levels: independent ambulation (GMFCS I-II), assisted ambulation (GMFCS III), and non-ambulation (GMFCS IV-V).

Explanatory variable

The patient's data included for the present study were as follows: prognostic predictors (age, type of CP, sitting independently at age two, and eating independently)[20] and other variables (gender, body mass index, caregivers, gestational age, birth weight, hyperbilirubinemia, epilepsy or seizure, intellectual impairment, visual impairment, hearing impairment, hand function, speech, medication, history of orthopedic surgery, and orthotics use). These variables were confirmed and the GMFCS was assessed using interviews on site, telephone, or mail.

Statistical analysis

The authors selected 471 cases having complete significant predictors' values for analyses. An adequate sample size was considered that at least 10 to 15 subjects per predictor should be included in the study[22]. For this reason, the present study had an adequate sample with 471 subjects, and the final model contained 10 variables. Then, the subjects were categorized into three groups by their GMFCS: independent ambulation, assisted ambulation, and non-ambulation (criterion-classified ambulatory

status). Baseline characteristics and clinical histories data were described by descriptive statistics: frequencies and percentages for categorical data, mean, and standard deviation for continuous data. The different data between the three groups were tested using the nonparametric test for trends across the ordered groups.

Multivariable ordinal continuation ratio logistic regression was used to analyze after the candidate predictors (p-value ≤0.20) were selected through univariable analysis. Coefficients of the significant predictors from multivariable models were converted into scores by division of the lowest coefficient, and they were rounded off to the nearest integer or half. The items and the total scores for each subject were created and used to represent the summary measure for predicting the ambulatory status in children with CP, and these were categorized into three levels (score-classified ambulatory status).

The discriminative and predictive abilities of the ambulatory status scores were presented with probability curves. The receiver operating characteristic (ROC) curve which was used to assess the probability of the total score showed ambulation. The Hosmer and Lemeshow Chi-square goodness-of-fit test[23] was made use to compare how well the predicted probabilities fit with the actual probabilities. Score-classified ambulatory statuses were compared to criterion-classified ambulatory statuses to indicate the estimation validity by percentage of agreement. All the analyses were performed using STATA statistical software Release 11.0 (Stata Corporation, College Station, TX) and those values for which p-value <0.05 were considered significant.

Results

There were 533 children with CP who were included in the current study, but we found missing values for some significant predictors in 62 subjects (11.6%), the remaining 471 subjects were considered for the data analysis. These missing predictors were type of CP (5.6%), and sitting independently at age two (6.2%). The subjects were classified into three groups according to their GMFCS levels: non-ambulation (n = 264), assisted ambulation (n = 57), and independent ambulation (n = 150) as illustrated in Fig. 1. Baseline characteristics and clinical histories, as illustrated in Table 1, showed that there were similarities as regards gender, caregivers, gestational age, birth weight, hyperbilirubinemia, intellectual impairment, hearing impairment, and orthotics use between the three groups.

In multivariable analysis, the significant predictors were age, type of CP, sitting independently at age two, and eating independently. Item scores for the significant predictors of the ambulatory status were derived from the coefficients. They varied from 0 to 6, and the total scores ranged from 0 to 12, as illustrated in Table 2. Fig. 2 demonstrated a simple score chart for predicting the ambulatory status, in which the subjects were classified into three groups according to their total scores: non-ambulation (scores <7), assisted ambulation (scores 7 to 8), and independent ambulation (scores >8). The author's scores predicted the non-ambulation group correctly in 244 out of 264, assisted ambulation in 10 out of 57, and independent ambulation in 113 out of 150. The prognostic estimation validity of the subjects into their original levels had a correctness percentage of 77.9%, underestimation had a correctness percentage of 12.1%, and overestimation had a correctness percentage of 10%, as illustrated in Table 3.

The distributions of the ambulatory status were presented with mean total scores: 3.4±2.5 in non-ambulation, 7.5±2.0 in assisted ambulation, and 9.2±1.8 in independent ambulation, as shown in Table 3. Fig. 3 illustrated the probability curves of the ambulatory status scores, which discriminate the non-ambulation group from the other groups (area

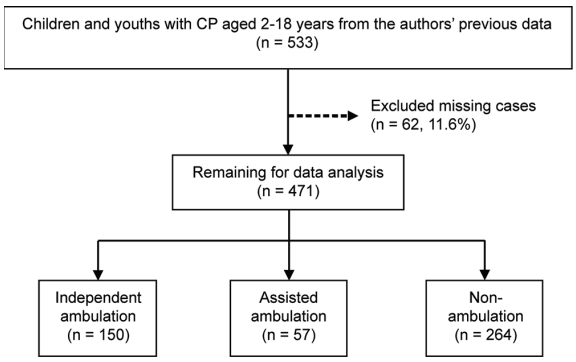

Fig. 1 Flow chart of data in the study.

Ambulatory prognostic score chart			
Predictors		Scores	
Age (year)	2 to less than 6	0	.....
	6 to less than 12	1	
	12 to 18	1.5	
Type of CP	Spastic quadriplegia	0	.....
	Mixed	2	
	Hypotonia	3	
	Spastic diplegia	3	
	Dyskinesia	3.5	
	Spastic hemiplegia	5	
	Ataxia	6	
Sitting independently at age 2		3	.....
Eating independently		1.5	.....
			+
	Total scores	0 to 12	.....

Total scores	Ambulatory status
<7	Non-ambulation
7 to 8	Assisted ambulation
>8	Independent ambulation

Fig. 2 The ambulatory prognostic score chart for children with cerebral palsy.

Table 1. Baseline characteristics and clinical histories of children with cerebral palsy

Variable	All subjects* (n = 471)	Non-ambulation* (n = 264)	Assisted ambulation* (n = 57)	Independent ambulation* (n = 150)	*p*-value#
Age (year)	10.1±4.3	9.2±4.2	10.9±4.0	11.4±4.1	<0.001
Male gender	272 (57.8)	147 (55.7)	34 (59.7)	91 (60.7)	0.312
Body mass index (kg/m^2) (n = 407)	15.6±3.5	15.0±3.4	16.3±4.4	16.2±3.1	<0.001
Parents caregiver	345 (73.3)	189 (71.6)	41 (71.9)	115 (76.7)	0.293
Type of CP					<0.001
Spastic quadriplegia	136 (28.9)	130 (49.2)	5 (8.8)	1 (0.7)	
Spastic diplegia	131 (27.8)	59 (22.3)	31 (54.4)	41 (27.3)	
Spastic hemiplegia	109 (23.2)	15 (5.7)	12 (21.0)	82 (54.7)	
Dyskinesia	50 (10.6)	32 (12.2)	3 (5.3)	15 (10.0)	
Ataxia	10 (2.1)	0 (0)	2 (3.4)	8 (5.3)	
Hypotonia	9 (1.9)	7 (2.7)	1 (1.8)	1 (0.7)	
Mixed	26 (5.5)	21 (7.9)	3 (5.3)	2 (1.3)	
Gestational age (week) (n = 453)	35.5±4.2	35.5±4.2	34.7±4.7	35.8±3.8	0.720
Birth weight (kg) (n = 451)	2.5±0.8	2.5±0.8	2.3±0.8	2.5±0.8	0.655
No Hyperbilirubinemia (n = 453)	347 (76.6)	195 (76.5)	46 (83.6)	106 (74.1)	0.694
No Epilepsy/seizure (n = 468)	250 (53.4)	124 (47.2)	42 (73.7)	84 (56.8)	0.028
Sitting independently at age 2	188 (39.9)	29 (11.0)	35 (61.4)	124 (82.7)	<0.001
No intellectual impairment	376 (79.8)	217 (82.2)	46 (80.7)	113 (75.3)	0.100
No visual impairment	406 (86.2)	214 (81.1)	52 (91.2)	140 (93.3)	<0.001
No hearing impairment	452 (96.0)	253 (95.8)	53 (93.0)	146 (97.3)	0.535
Have functional use of hands	385 (81.7)	181 (68.6)	56 (98.3)	148 (98.7)	<0.001
Eating independently	278 (59.0)	96 (36.4)	50 (87.7)	132 (88.0)	<0.001
Speech (says single words, sentences)	276 (58.6)	111 (42.1)	46 (80.7)	119 (79.3)	<0.001
Medication history (n = 466)	349 (74.9)	213 (81.6)	34 (59.7)	102 (68.9)	0.002
Orthopedic surgery (n = 460)	53 (11.5)	19 (7.3)	12 (21.1)	22 (15.4)	0.008
Orthotics use (n = 458)	167 (36.5)	94 (35.7)	27 (48.2)	46 (33.1)	0.763

CP = cerebral palsy; SD = standard deviation

* Values represent n (%) for categorical data and mean ± SD for continuous data

Trend test across the ordered groups

Table 2. Item score for significant predictors of ambulatory status (n = 471)

Predictors	OR (95% CI)*	*p*-value*	Coefficient*	Scores
Age (year)				
2 to less than 6	Reference		Reference	0
6 to less than 12	2.07 (1.07 to 3.98)	0.030	0.73	1
12 to 18	3.26 (1.59 to 6.72)	0.001	1.18	1.5
Type of CP				
Spastic quadriplegia	Reference		Reference	0
Mixed	3.94 (1.09 to 14.25)	0.037	1.37	2
Hypotonia	9.76 (1.89 to 50.39)	0.007	2.28	3
Spastic diplegia	8.07 (3.27 to 19.95)	<0.001	2.09	3
Dyskinesia	12.09 (4.42 to 33.04)	<0.001	2.49	3.5
Spastic hemiplegia	40.47 (15.37 to 106.56)	<0.001	3.70	5
Ataxia	91.49 (15.26 to 548.58)	<0.001	4.52	6
Sitting independently at age 2				
No	Reference		Reference	0
Yes	7.74 (4.85 to 12.34)	<0.001	2.05	3
Eating independently				
No	Reference		Reference	0
Yes	2.95 (1.65 to 5.24)	<0.001	1.08	1.5

CI = confidence interval; CP = cerebral palsy; OR = odds ratio

* Analysis using multivariable ordinal continuation ratio logistic regression

Table 3. Score-classified ambulatory status, criterion-classified ambulatory status, and prognostic estimation validity

Score-classified ambulatory status	Total score	Criterion-classified ambulatory status			Validity*		
		Non-ambulation	Assisted ambulation	Independent ambulation	% over	% correct	% under
Mean ± SD		3.4±2.5	7.5±2.0	9.2±1.8			
IQR		1 to 5.5	6 to 9	8.5 to 10.5			
Non-ambulation (n = 284)	<7	244	20	20	-	51.8	8.5
Assisted ambulation (n = 34)	7 to 8	7	10	17	1.5	2.1	3.6
Independent ambulation (n = 153)	>8	13	27	113	8.5	24.0	-
Total (n = 471)	0 to 12	264	57	150	10.0	77.9	12.1

IQR = interquartile range; SD = standard deviation
* Percentage of total subjects

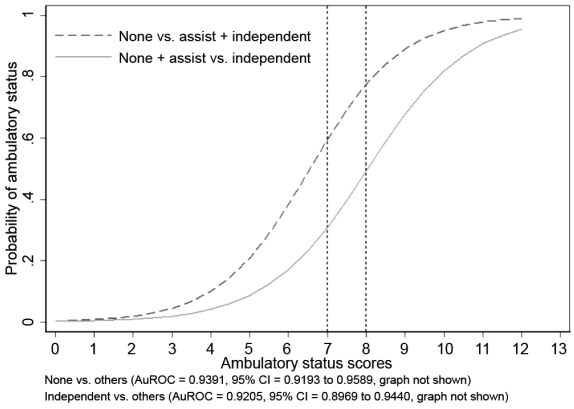

Fig. 3 The discrimination of the ambulatory status scores.

under the receiver operating characteristic curve; AuROC = 0.9391, graph not shown), and discriminate the independent ambulation group from the other groups (AuROC = 0.9205, graph not shown).

Discussion

This is the first development of a simple ambulatory score chart of Thai children with CP based on the operational definition outcome from GMFCS. It was constructed using routine data including age, type of CP, sitting independently at the age of two, and eating independently. The ambulatory status was classified into three levels according to their GMFCS and total score: independent ambulation, assisted ambulation, and non-ambulation. The ability to predict ambulation in these children appeared accurate, with 77.9% of correctness and high discrimination with AuROC more than 0.9.

The authors' prognostic tool is different from the previous tools in both outcome and predictors, including techniques and applications. The significant predictors of this score chart have been mentioned in the authors' previous study[20]. It is well known that age or maturation is associated with different aspects of child development including walking[17]. The type of CP and gross motor skills (sitting independently) were found to have a strong association with ambulation in several previous studies for a long time[4,5,9,10,13,17,24,25]. In addition, it had been recently found that eating independently was associated with ambulation in two previous studies[5,13]. Nevertheless, strong predictors such as primitive reflexes and postural reactions were excluded from the present study because the authors took into consideration of predictors from routine data to clinical usefulness.

The ambulatory prognostic score chart was developed for the simple use of clinicians and therapists. The ambulatory outcome was divided into three groups, which may be useful for clinical practice. The first group, of children scoring <7, was classified as the 'non-ambulation' group. The health care team should inform the parents that the children could not walk in the first age range, and the team should have a treatment plan chalked out with the parents to improve the walking ability of the children to bring it to its full potential. If the children were more likely to continue as having non-ambulation in the next age, their parents should plan to adjust the environmental context and the daily life of the children with assistive devices. The second group, with the children scoring from 7 to 8, was classified as the 'assisted ambulation' group. In the first stage, these children were assisted to walk with aids such as wheel walkers, but when they grow up, there might be a possibility that the children will walk independently. Thus, the health care team should plan for parents to emphasize the enhancement of the children's walking ability. The last group, of children scoring >8, was classified as the 'independent ambulation' group. These children could walk

independently before six years of age, so an appropriate treatment plan would be to maintain the walking ability and the cardiopulmonary fitness of the children or to encourage social participation. When children with CP grow into adolescence, they may effectively experience a decline in the walking ability. However, the present data show that adolescents with CP aged 12 to 18 succeeded in walking in comparison with children with CP aged 2 to 6 (OR = 3.26; 95% CI = 1.59 to 6.72). There are studies that support the possibility that some children with CP continue to maintain and develop the walking ability into adolescence[5,26-28]. On the other hand, Kerr et al[29] point out that the lowest effective walking ability is at about 12 years of age, and that deterioration of the gross motor skill takes over after the age of 13. This issue in adolescence remains unclear. However, in adults, it has been reported that when children with CP grow into adulthood (>20 years), they have the potential to experience walking decline due to fatigue, inefficiency of ambulation, or increased joint pains[27,30].

For instance, the sum scores for a child with spastic diplegia (score = 3) aged four (score = 0) who can sit independently before age two (score = 3) and eats independently now (score = 1.5) is 7.5 (0+3+3+1.5, see Fig. 1). This means that in the period of age ranging from 2 years to 6 years, he is able to walk with assistive devices. When he grows up (score = 1, for the age range 6 to 12), the sum scores will have one point added, as 8.5 (1+3+3+1.5, see Fig. 1), which means that he has a chance to walk independently. However, the present data still had 10% of overestimation (children were detected as over true ambulatory levels) and 12.1% of underestimation (children were detected as under true ambulatory levels) which can be the result of other predictors, such as primitive reflexes, not being taken into consideration for the analyses, but this is acceptable. So, this tool is reliable for the prediction of the ambulatory status in children with CP. Additionally, the discriminative and predictive abilities of the authors' tool showed that the performance of the model was good.

Some limitations of the present study need to be mentioned. First, the routine data had some of the predictors missing; however, the authors assumed that they were missing completely at random. Consequently, we confirm that the data collection was unbiased. Second, primitive reflex and postural reaction, which are associated with ambulatory status, were excluded from the present study since it is not routine data. Finally, this score chart may be restricted, in generalization to other contexts, because it was constructed from routine clinical practice of the settings in northeastern and northern Thailand. These settings are in the form of hospitals or special schools for children with physical disability that the parents take their children to for treatment when they find their children encountering problems with regard to carrying out normal functions, routine functions which these children are unable to perform since birth. Some children with CP who walk independently, may not be discovered in the present study. Thus, this prognostic tool holds potential and should be externally validated in a different setting before utilization in clinics.

In conclusion, a simple ambulatory prognostic score chart was derived from age, type of CP, sitting independently at the age of two, and eating independently, which shows high discriminative values of ambulatory status in children with CP. However, the validation of this score chart should be tested in other subjects before clinical practice application.

What is already known on this topic?

Type of CP, sitting independently at age two, and eating independently are prognostic predictors for ambulation in children with CP. Age is associated with ambulation in children with CP.

What this study adds?

The ambulatory prognostic score chart is developed from age, type of CP, sitting independently at the age of two, and eating independently can predict ambulatory status in Thai children with CP aged 2 to 18 years.

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Potential conflicts of interest

None.

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การสร้างแผนภูมิคะแนนทำนายการเดินสำหรับเด็กไทยสมองพิการ อายุ 2 ถึง 18 ปี

อรวรรณ กีรติสิโรจน์, นวลลออ ธวินชัย, มนธนา บุญตระกูลพูนทวี, วัณทนา ศิริธราธิวัตร

ภูมิหลัง: *ผู้ปกครองส่วนใหญ่ต้องการทราบว่าบุตรของพวกเขาซึ่งมีภาวะสมองพิการจะเดินได้หรือไม่ ประเทศไทยยังขาดเครื่องมืออย่างง่ายที่ใช้ทำนายสถานะการเดินซึ่งใช้คำจำกัดความของการเดินด้วย Gross Motor Function Classification System*

วัตถุประสงค์: *เพื่อสร้างแผนภูมิคะแนนทำนายอย่างง่ายสำหรับทำนายสถานะการเดินในเด็กไทยสมองพิการ*

วัสดุและวิธีการ: *เด็กสมองพิการอายุ 2 ถึง 18 ปี จำนวนทั้งหมด 471 คน ซึ่งลงทะเบียนและรับการรักษาที่โรงเรียนการศึกษาพิเศษ หรือ โรงพยาบาลสำหรับเด็กที่บกพร่องทางการเคลื่อนไหว ระหว่าง พ.ศ. 2551 ถึง พ.ศ. 2556 จำนวน 6 แห่ง ได้รับการคัดเลือก ผู้นิพนธ์เก็บรวบรวมข้อมูลทั่วไปและประวัติทางคลินิกของเด็กสมองพิการจากเวชระเบียน สถานะการเดินถูกจำแนกเป็น 3 มาตราอันดับ โดย Gross Motor Function Classification System - Expanded and Revised version*

ผลการศึกษา: *การวิเคราะห์ ordinal continuation ratio logistic regression แบบหลายตัวแปรบ่งชี้ว่า อายุ ชนิดของสมองพิการ การนั่งได้เองเมื่ออายุ 2 ปี และการกินได้เอง คือ ปัจจัยทำนายสำคัญของการเดิน รายการเหล่านี้ถูกนำมารวมกันเป็นคะแนนการทำนายทางคลินิก ได้แก่ เดินไม่ได้ (น้อยกว่า 7 คะแนน) เดินโดยการช่วยเหลือ (7 ถึง 8 คะแนน) และเดินได้เองโดยอิสระ (มากกว่า 8 คะแนน)*

สรุป: *เครื่องมือทำนายมีค่าการจำแนกสถานะการเดินในกลุ่มเด็กสมองพิการสูง อย่างไรก็ตามการตรวจสอบความตรงของเครื่องมือนี้ต้องการการทดสอบในตัวอย่างกลุ่มอื่น ก่อนนำไปประยุกต์ใช้ในทางคลินิก*
