Risk factors of strabismus surgery among pediatric cerebral palsy population with strabismus in Taiwan: A population-based cohort study

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Abstract

Background: To identify the risk factors of strabismus surgery among Taiwanese children with severe cerebral palsy (CP) and strabismus.

Methods: This retrospective nationwide population-based cohort study examined a cohort of newly diagnosed pediatric CP patients (age ≤ 10 y) between 1997 and 2013 with strabismus. The primary endpoint was strabismus surgery. A stepwise logistic regression was applied to determine the demographic factors, ophthalmic conditions, and comorbidities associated with strabismus surgery.

Results: Out of 808 patients, 115 had received strabismus surgery. The significant factors correlated to strabismus surgery in pediatric patients with severe CP and strabismus were CP diagnosis age < 4 years, residency in a suburban/rural area, low birth weight, and strabismic amblyopia.

Conclusion: In CP children with strabismus who have risk factors of younger CP diagnosis age (age < 4 y), residency in a suburban/rural area, a low birthweight, and the presence of strabismic amblyopia, strabismus surgery should be considered.

Keywords: Cerebral palsy; Cohort study; Intervention; Strabismus

1. INTRODUCTION

Cerebral palsy (CP) is an important global public health issue and the most common physical disability in early childhood.[1–3] The worldwide prevalence of CP is approximately 2-2.5 per 1000 live births[2] and the incidence of CP is about one to four cases per 1000 live births.[4] Ophthalmological disorders are some of the most frequent problems associated with severe CP,[5] including significant refractive errors, strabismus, nystagmus, and amblyopia as well as cortical visual impairment.[5,6] Strabismus is more common in children with CP than neurologically normal children,[7] with an incidence varying from 20% to 90% in the literature.[6,8–14] However, comprehensive ophthalmic examination is difficult in CP patients. The treatment and response for strabismus in CP patients is not well studied and few specific guidelines have been outlined in the ophthalmic literature. Strabismus when found in CP patients should be treated promptly to prevent amblyopia. Strabismus surgery should be considered in CP patients for psychosocial reasons as well as for the potential successful realignment and restoration of binocular vision.[8,10] In this study, we aim to identify the factors associated with strabismus surgery based on administrative data about the population in Taiwan.

2. METHODS

2.1. Data source

The data used in this study were from the Taiwan National Health Insurance Research Database (NHIRD), released by the National Research Institutes for research purposes. Taiwan's National Health Insurance was established in 1995. This single universal national health insurance program covers 99.6% of the population up to 2011. The advantages of using the NHIRD for research purposes have been described in previous literature.[15] All registry data in the NHIRD consist of demographic characteristics, all types of medical visits, diagnostic codes, laboratory test codes, procedure codes, prescription codes, and the medical costs for reimbursement. This study was approved by the Institutional Review Board of Kaohsiung Veterans General Hospital, Kaohsiung in Taiwan (VGHKS15-CT12-01). Because all personal identifications have been replaced with surrogate numbers, no informed consent was required from the study

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Conflicts of interest: The authors declare that they have no conflicts of interest related to the subject matter or materials discussed in this article.

Journal of Chinese Medical Association. (2020) 83: 1107-1110.

Received December 26, 2019; accepted February 29, 2020.

doi: 10.1097/JCMA.0000000000000440.

population for the present study. The NHIRD had Registry for Catastrophic Illnesses Patient Database (RCIPD), which enrolled approximately 30 diseases including CP.

2.2. Study cohort

This study is a retrospective cohort study analyzing newly diagnosed pediatric CP patients (≤ 10 y old) with a strabismus diagnosis from 1997 to 2013.

2.3. Definition of severe CP

We included patients that met the criteria for CP in the catastrophic illness certificate system, who were coded by the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) 343.x. In Taiwan, only the patients proven to have a definite CP diagnosis and a moderate to severe physical or mental disability classification by the designated hospitals can apply for a catastrophic illness certificate. To obtain a catastrophic illness certificate, CP diagnosis must be confirmed by either a neurologist or rehabilitation physician and then verified by the National Health Insurance Administration.

The children were diagnosed with strabismus on the basis of the strabismus diagnostic codes 378.00, 378.10, 378.20, and 378.30 (ICD-9-CM).

The exclusion criteria for this study were as follows: (1) CP catastrophic illness certificate approved at age > 11 years and (2) patient data in the database is incomplete. The index date was defined as the first date of CP catastrophic illness certification.

2.4. Outcomes and predictor variables

The primary outcome is strabismus surgery, using the procedure codes (86601C, 86602C, 86603C, 86604C, 86605C). The patients' sociodemographic characteristics, including the CP diagnosis age (base on RCIPD), sex, and residential area, were obtained from their initial enrollment data. Urban, suburban, and rural area were defined according to Liu et al,[16] using population density, the percentage of residents with college level or higher education, the percentage of residents, residents of agriculture workers, number of physicians per 100 000 residents.

The comorbidities and eye conditions before or after CP diagnosis found in the RCIPD were as follows: strabismus diagnosis age, amblyopia (ICD-9-CM codes 368.00, 368.01, 368.02, 368.03), retinopathy of prematurity (ICD-9-CM codes 362.20, 326.21), low birth weight (ICD-9-CM codes 765.1), epilepsy (ICD-9-CM codes 345), and orthopedic surgeries (procedure codes 64006B, 64260B, 64064B).

2.5. Statistical analysis

The study groups were compared using a chi-square test for categorical variables, and continuous variables were analyzed using one-way analysis of variance. The multivariable logistic regression model was used to assess variables associated with strabismus surgery, taking into account the patients' demographic characteristics and comorbidities.

All statistical tests were performed using Statistical Analysis Software (SAS) version 9.4 (SAS System for Windows) and SPSS (version 20; SPSS Inc., Chicago, IL, USA). A p value of less than 0.05 was considered statistically significant.

3. RESULTS

The baseline characteristics of each group are summarized in Table 1. A total of 808 patients with CP and strabismus were included, in which 115 (14.2%) received strabismus surgery. The mean age of CP diagnosis in the strabismus surgery group was significantly younger than in the nonsurgery group (2.86 vs 4.01 y). There was no significant difference between the two groups in terms of strabismus diagnosis age, gender, residence, the presence of amblyopia, previous orthopedic surgery, or Charlson Comorbidity Index. The percentage of patients with low birth weight, retinopathy of prematurity, and strabismic amblyopia were significantly higher in the surgery group (62% vs 45%; p = 0.001, 29% vs 18%; p = 0.01, and 6% vs 2%; p = 0.011). The percentage patients with epilepsy was significantly higher in the nonsurgery group than in the surgery group (44% vs 33%; p = 0.032).

After univariate logistic regression analysis, the CP diagnosis age ≤ 3.85 years (odds ratio [OR], 2.48; 95% CI, 1.52-4.04; p=0.001), low birth weight (OR, 1.994; 95% CI, 1.33-2.99; p = 0.001), retinopathy of prematurity (OR, 1.79; 95% CI, 1.15-2.81; p = 0.011), absence of epilepsy (OR, 1.57; 95% CI, 1.04-2.39; p = 0.033), and strabismic amblyopia (OR, 3.14; 95% CI 1.24-7.97; p = 0.016) were all associated with strabismus surgery (Table 2).

Table 1

Baseline characteristics of cerebral palsy patients with strabismus (n = 808)

Variables	Nonoperation, n = 693 (%)	Operation, n = 115 (%)	p
CP diagnosis age, y, mean ± SD	4.01 ± 3.0	2.86 ± 2.98	< 0.001
Strabismus diagnosis age, y, mean ± SD	2.01 ± 2.2	1.93 ± 2.1	0.525
Gender			0.244
Female	315 (45)	59 (51)	
Male	378 (55)	56 (49)	
Hospital characteristics			0.328
Medical center	431 (62)	77 (67)	
Regional/others	262 (38)	38 (33)	
Region			0.636
North	369 (53)	60 (52)	
Middle	155 (22)	30 (26)	
South/others	169 (25)	25 (22)	
Urbanization			0.105
Urban	434 (63)	82 (71)	
Suburban	213 (31)	30 (26)	
Rural	43 (6)	3 (3)	
Orthopedic surgery			0.564
No	691 (99)	115 (100)	
Yes	2 (1)	0 (0)	
Amblyopia			0.638
No	538 (78)	87 (76)	
Yes	155 (22)	28 (24)	
Low birth weight			0.001
No	383 (55)	44 (38)	
Yes	310 (45)	71 (62)	
Retinopathy of prematurity			0.010
No	566 (82)	82 (71)	
Yes	127 (18)	33 (29)	
Epilepsy			0.032
No	390 (56)	77 (67)	
Yes	303 (44)	38 (33)	
Pneumonia			0.712
No	302 (44)	48 (42)	
Yes	391 (56)	61 (58)	
CCIS			0.100
0	572 (83)	102 (89)	
≥ 1	121 (17)	13 (11)	
Strabismic amblyopia			0.011
No	679 (98)	108 (94)	
Yes	14 (2)	7 (6)	

CCIS = Charlson Comorbidity Index Score; CP = cerebral palsy.

Table 2

Univariate logistic regression analysis for cerebral palsy patients with strabismus operation

Variables	Beta	OR (95% CI)	*p*
CP diagnosis age (median =3.85 y)			
≤ 3.85 y	0.907	2.48 (1.52-4.04)	< 0.001
> 3.85 y		1	
Strabismus diagnosis age (median = 1.3 y)			
≤ 1.3 y	0.154	1.12 (1.52-4.04)	0.446
> 1.3 y		1	
Gender			
Female	0.235	1.26 (0.85-1.88)	0.242
Male		1	
Hospital characteristics (teaching level)			
Medical center		1	
Regional/others	0.208	1.23 (0.81-1.87)	0.328
Region			
North	0.095	1.10 (0.67-1.81)	0.711
Middle	0.269	1.31 (0.74-2.32)	0.359
South/others		1	
Urbanization			
Urban		1	
Suburban/rural	0.394	1.48 (0.96-2.29)	0.074
Orthopedic surgery			
No		1	
Yes	...	...	...
Amblyopia			
No		1	
Yes	0.111	1.12 (0.70-1.77)	0.638
Low birth weight			
No		1	
Yes	0.690	1.994 (1.33-2.99)	0.001
Retinopathy of prematurity			
No		1	
Yes	0.584	1.79 (1.15-2.81)	0.011
Epilepsy			
No	0.454	1.57 (1.04-2.39)	0.033
Yes		1	
Pneumonia			
No		1	
Yes	0.075	1.08 (0.72-1.61)	0.712
CCIS			
0	0.507	1.66 (0.90-3.05)	0.103
≥ 1		1	
Strabismic amblyopia			
No		1	
Yes	1.145	3.14 (1.24-7.97)	0.016

CCIS = Charlson Comorbidity Index Score; CP = cerebral palsy; OR = odds ratio.

On subsequent multivariate stepwise logistic regression, four independent parameters associated with strabismus surgery were identified: CP diagnosis age ≤ 3.85 years (OR, 2.29; 95% CI, 1.39-3.78; p = 0.001), residence in a suburban/rural area (OR, 1.67; 95% CI, 1.07-2.60; p = 0.025), low birth weight (OR, 1.82; 95% CI, 1.20-2.75; p = 0.005), and strabismic amblyopia (OR, 3.34; 95% CI, 1.29-8.67; p = 0.013) (Table 3).

Table 3

Stepwise logistic regression analysis for strabismic cerebral palsy patients with strabismus operation

Variables	Beta	OR (95% CI)	*p*
CP diagnosis age (median = 3.85 y)			
≤ 3.85 y	0.830	2.29 (1.39-3.78)	0.001
> 3.85 y		1	
Urbanization			
Urban		1	
Suburban/rural	0.511	1.67 (1.07-2.60)	0.025
Low birth weight			
No		1	
Yes	0.597	1.82 (1.20-2.75)	0.005
Strabismic amblyopia			
No		1	
Yes	1.206	3.34 (1.29-8.67)	0.013

CP = cerebral palsy; OR = odds ratio.

4. DISCUSSION

To the best of our knowledge, this is the first cohort study using a nationwide population-based data set to identify risk factors for strabismus surgery in children with severe CP and strabismus. Our risk classification was based on the ophthalmic conditions, medical comorbidities, and sociodemographic factors. The major finding of this nationwide population-based cohort study is that CP diagnosis age < 4 years, residency in a suburban/rural area, a low birth weight, and strabismic amblyopia were significant factors associated with strabismus surgery among this pediatric population with severe CP and strabismus.

This study has several merits. Our nationwide population-based cohort study included CP with strict inclusion criteria. We used simple baseline demographics and clinical factors to identify patients with a high probability of strabismus surgery and could be used to improve the treatment strategy of pediatric CP patients.

In our study, most of the patient (85.8%) did not receive strabismus surgery. This may reflect that in Taiwan, most surgeons tend to approach treating CP patients conservatively. In our study, we included patients with severe CP, who are more likely to have multiple medical comorbidities and thus have higher risk of surgery under general anesthesia. Our literature review showed a variable percentage of pediatric CP patients undergoing strabismus surgery, ranging from 20.5% to 76%.[6,10,14] Some argue that nonsurgical treatment is more appropriate in CP patients for multiple reasons such as the difficulty in measuring the angle of strabismus, the high rates of surgical overcorrection, and decreased fusional ability.[17,18]

A patient with a CP diagnosis age < 4 years is significantly associated with strabismus surgery in our study. Early CP diagnosis is associated with a higher degree of motor disability.[19] Clinically speaking, it is quite reasonable, because the recognition of the abnormal motor pattern may prompt earlier examination. Jeon et al[20] found that strabismus is more prevalent in the severe motor impairment CP children (Gross Motor Function Classification System level 4-5). However, due to the limitation of our NHIRD system, we could not access the motor function of our patients.

Residency in a suburban/rural area is significantly associated with strabismus surgery in our study. Previous studies have suggested that rural residents were more likely to receive surgical procedures.[21] In Taiwan, strabismus surgery is mostly done in medical centers in urban cities. Compared with urban residency, suburban/rural residency maybe more likely to opt for surgical treatment to resolve medical problems instead of putting up with multiple inconvenient medical visits.

The risk of CP is higher in infants with a low birth weight than in infants of normal birthweight.[22] Increased prevalence of strabismus in the low birth weight population has been reported in several studies.[23–25] Children born with very low birth weights also have an increased frequency of refractive errors and amblyopia.

Strabismic amblyopia has been found to be caused by active inhibition of the retinocortical pathways of visual input originating in the fovea of the deviating eye.[26] Birch et al[27] conducted a prospective study following children with infantile esotropia and concluded that early surgical intervention (before 6 months old) may be beneficial in promoting binocular function, including improvements in fusion and stereopsis for children with infantile esotropia. Spontaneous improvement of amblyopia has been seen simply with ocular alignment after strabismus surgery.[28]

There were several limitations when interpreting the results of this study. First, the gross motor function classification system level, which is an indicator of a poor level of motor function, is not accessible in the Taiwan NHIRD system. Second, we cannot obtain data on the deviation angle of strabismus, visual acuity, or refractive errors.

In conclusion, a younger CP diagnosis age (age < 4 y), residency in suburban/rural area, a low birthweight, and the presence of strabismic amblyopia are all associated with strabismus surgery in pediatric CP patients with strabismus. An early ophthalmic examination and strabismus surgery should be considered in these patients for potential successful ocular realignment and the restoration of binocular vision. An early ophthalmic examination is recommended for pediatric CP patients with strabismus to start management.

REFERENCES

1. Gulati S, Sondhi V. Cerebral palsy: an overview. *Indian J Pediatr* 2018;**85**:1006–16.
2. Oskoui M, Coutinho F, Dykeman J, Jetté N, Pringsheim T. An update on the prevalence of cerebral palsy: a systematic review and meta-analysis. *Dev Med Child Neurol* 2013;**55**:509–19.
3. Stavsky M, Mor O, Mastrolia SA, Greenbaum S, Than NG, Erez O. Cerebral palsy-trends in epidemiology and recent development in prenatal mechanisms of disease, treatment, and prevention. *Front Pediatr* 2017;**5**:21.
4. Boel L, Pernet K, Toussaint M, Ides K, Leemans G, Haan J, et al. Respiratory morbidity in children with cerebral palsy: an overview. *Dev Med Child Neurol* 2019;**61**:646–53.
5. Fazzi E, Signorini SG, LA Piana R, Bertone C, Misefari W, Galli J, et al. Neuro-ophthalmological disorders in cerebral palsy: ophthalmological, oculomotor, and visual aspects. *Dev Med Child Neurol* 2012;**54**:730–6.
6. Hiles DA. Results of strabismus therapy in cerebral palsied children. *Am Orthopt J* 1975;**25**:46–55.
7. Ma DJ, Yang HK, Hwang JM. Surgical outcomes of medial rectus recession in esotropia with cerebral palsy. *Ophthalmology* 2013;**120**:663–7.
8. Ghasia F, Brunstrom J, Gordon M, Tychsen L. Frequency and severity of visual sensory and motor deficits in children with cerebral palsy: gross motor function classification scale. *Invest Ophthalmol Vis Sci* 2008;**49**:572–80.
9. Dufresne D, Dagenais L, Shevell MI; REPACQ Consortium. Spectrum of visual disorders in a population-based cerebral palsy cohort. *Pediatr Neurol* 2014;**50**:324–8.
10. Jackson J, Castleberry C, Galli M, Arnoldi KA. Cerebral palsy for the pediatric eye care team part II: diagnosis and treatment of ocular motor deficits. *Am Orthopt J* 2006;**56**:86–96.
11. Collins ML. Strabismus in cerebral palsy: when and why to operate. *Am Orthopt J* 2014;**64**:17–20.
12. Han SY, Han J, Han SH, Lee JB, Rhiu S. Ocular alignment after bilateral lateral rectus recession in exotropic children with cerebral palsy. *Br J Ophthalmol* 2015;**99**:757–61.
13. Breakey AS. Ocular findings in cerebral palsy. *AMA Arch Ophthalmol* 1955;**53**:852–6.
14. Woo SJ, Ahn J, Park MS, Lee KM, Gwon DK, Hwang JM, et al. Ocular findings in cerebral palsy patients undergoing orthopedic surgery. *Optom Vis Sci* 2011;**88**:1520–3.
15. Hsing AW, Ioannidis JP. Nationwide population science: lessons from the Taiwan National Health Insurance Research Database. *JAMA Intern Med* 2015;**175**:1527–9.
16. Liu CY, Hung YT, Chuang YL. Incorporating development stratification of Taiwan townships into sampling design of large scale health interview survey. *J Health Manag* 2006;**4**:1–22.
17. Bang GM, Brodsky MC. Neurological exotropia: do we need to decrease surgical dosing? *Br J Ophthalmol* 2013;**97**:241–3.
18. Ma DJ, Yang HK, Hwang JM. Surgical responses and outcomes of bilateral lateral rectus recession in exotropia with cerebral palsy. *Acta Ophthalmol* 2017;**95**:e179–84.
19. Granild-Jensen JB, Rackauskaite G, Flachs EM, Uldall P. Predictors for early diagnosis of cerebral palsy from national registry data. *Dev Med Child Neurol* 2015;**57**:931–5.
20. Jeon H, Jung JH, Yoon JA, Choi H. Strabismus is correlated with gross motor function in children with spastic cerebral palsy. *Curr Eye Res* 2019;**18**:1–6.
21. Francis ML, Scaife SL, Zahnd WE. Rural-urban differences in surgical procedures for Medicare beneficiaries. *Arch Surg* 2011;**146**:579–83.
22. Platt MJ, Cans C, Johnson A, Surman G, Topp M, Torrioli MG, et al. Trends in cerebral palsy among infants of very low birthweight (<1500 g) or born prematurely (<32 weeks) in 16 European centres: a database study. *Lancet* 2007;**369**:43–50.
23. O'Connor AR, Stephenson TJ, Johnson A, Tobin MJ, Ratib S, Fielder AR. Strabismus in children of birth weight less than 1701 g. *Arch Ophthalmol* 2002;**120**:767–73.
24. Schalij-Delfos NE, de Graaf ME, Treffers WF, Engel J, Cats BP. Long term follow up of premature infants: detection of strabismus, amblyopia, and refractive errors. *Br J Ophthalmol* 2000;**84**:963–7.
25. Sandfeld Nielsen L, Jensen H, Skov L. Risk factors of ophthalmic disorders in children with developmental delay. *Acta Ophthalmol* 2008;**86**:877–81.
26. Koo EB, Gilbert AL, VanderVeen DK. Treatment of amblyopia and amblyopia risk factors based on current evidence. *Semin Ophthalmol* 2017;**32**:1–7.
27. Birch EE, Fawcett S, Stager DR. Why does early surgical alignment improve stereoacuity outcomes in infantile esotropia? *J AAPOS* 2000;**4**:10–4.
28. Dadeya S, Kamlesh MS. Is it mandatory to treat amblyopia prior to surgery in esotropia? *Acta Ophthalmol Scand* 2001;**79**:28–30.