Clinical Studies

In-hospital complications after cervical fusion in cases with versus without cerebral palsy[☆]

Anoop R. Galivanche[a,b], Stephen M. Gillinov[a], Michael R. Mercier[a,c], Christopher A. Schneble[a], Arya G. Varthi[a], Jonathan N. Grauer[a], David B. Frumberg[a,*]

[a] *Department of Orthopaedics and Rehabilitation, Yale School of Medicine, 47 College Street, New Haven, CT 06511, USA*
[b] *Department of Orthopaedic Surgery, University of California, San Francisco School of Medicine, 500 Parnassus Avenue, San Francisco, CA, 94143 USA*
[c] *Division of Orthopaedics, Department of Surgery, University of Toronto, 149 College Street, Toronto, ON M5T 1P5 USA*

ABSTRACT

Background: Patients with cerebral palsy (CP) are at increased risk for cervical spine pathology. Cervical fusion surgery may be considered in this population, but perioperative outcomes relative to patients without CP remains poorly understood. The purpose of this study was to compare in-hospital complications after cervical fusion in patients with versus without cerebral palsy (CP) using a retrospective cohort design.
Methods: Cervical fusion cases with and without CP were identified in the National Inpatient Sample (NIS) database. In-hospital adverse events were tabulated and grouped into any (AAE), serious (SAE), and minor adverse events (MAE). Length of hospital stay (LOS) and mortality were assessed. Multiple logistic regression models with and without 1:1 propensity matching were used to compare outcomes between cases with and without CP, controlling for demographic and preoperative variables.
Results: After weighting, 1,518,012 cases were included in the study population, of which 4,554 (0.30%) had CP. Those with CP were younger, more often male, suffered more comorbidities, more frequently operated on from a posterior or combined approach, and were more frequently addressed at more than one level. By multiple logistic regression after matching, CP cases had higher odds of AAE (OR 1.72; 95% CI 1.05-2.81; p=0.030) and MAE (OR 2.07; 95% CI 1.20-3.57; p=0.009), but no differences in odds of SAE or in-hospital mortality.
Conclusions: As there is increasing awareness of potentially cervical pathology in the CP population, the current study suggests that surgical intervention for this population can be appropriately considered without severe in-hospital morbidity or mortality.

Introduction

Cerebral palsy (CP) is a heterogenous group of disorders affecting muscle tone and the development of movement and posture. Affecting approximately 2 out of every 1,000 live births in developed countries, CP is the most common motor disability amongst children [1–4].

There are multiple reasons CP can have cervical spine effects. Spasticity is found in approximately 75% of CP cases, with significant gait and musculoskeletal effects [5]. Dystonia and dyskinesia can be found in many [6–8]. A multidisciplinary approach is often employed throughout childhood to maximize function and quality of life, but regular muscu-

loskeletal surveillance is rare in adulthood throughout North America. It has thus been proposed that cervical spine pathology has been previously underrecognized in this population, perhaps because of the misattribution of symptoms to the natural course of CP [7].

Since Anderson et al first documented two cases of cervical myelopathy in CP patients, several case series have described the association between CP and cervical myelopathy [9,10]. Radiographic studies comparing the cervical spines of CP patients and non-CP patients have implicated listhetic instability, disc degeneration, and cervical stenosis in the pathogenesis of accelerated cervical spine degeneration in CP patients. [11] Motion analysis by Ebara et al found that CP patients engage in

---

neck flexion-extension at higher velocities than non-CP patients, thereby subjecting cervical articulations to greater stress [12].

While conservative measures are the mainstay of treatment for many cervical spine conditions, myelopathy in particular is typically considered for surgical intervention. Nonetheless, little information exists regarding the operative risk associated with performing cervical spinal fusions in patients with CP. Prior studies examining spinal fusion in CP patients have focused on factors such as long-term survival, patient satisfaction, and life expectancy [13,14].

Thus, the current study sought to leverage the statistical power of a large, national database to describe the demographics, clinical characteristics, and in-hospital postoperative complication profiles of CP cases undergoing cervical fusion surgery relative to those without CP.

Methods

Data source

The present study utilized a retrospective, cross-sectional design to analyze data from the 2008-2018 National Inpatient Sample (NIS). Our institution's Human Investigations Committee deemed this study Not Human Research because the data source only comprised de-identified patient information.

NIS is the largest longitudinal all-payer dataset of inpatient hospital episodes in the United States. After weighting to extrapolate the national sample to national numbers, more than 35 million hospitalizations are noted annually. The scale of the NIS data allows the study relatively small cohorts, for which single institution data may be inadequate.

Study population

The 2008-2018 NIS was queried for adult (greater than or equal to eighteen years of age) cases undergoing cervical spine surgeries using the International Classification of Diagnoses, 9th Revision (ICD-9) and ICD-10 procedure codes. Cases performed for degenerative indications were identified using ICD-9 and ICD-10 diagnostic codes. Cases performed for indications involving trauma, infection, and neoplasia, as well as non-elective cases were excluded.

Cases with CP were then identified using ICD-9 and ICD-10 diagnostic codes. Age and sex were directly abstracted from the dataset. Overall comorbidity burden of each case was approximated using Elixhauser Comorbidity Index (ECI) score and grouped into the following bins: 0 comorbidities, 1-5 comorbidities, and greater than 5 comorbidities.

Outcome variables

Length of hospital stay (LOS) and in-hospital mortality were directly abstracted from the dataset. In-hospital adverse events were assessed using ICD codes. These were then aggregated into: minor adverse event (MAE; pneumonia or urinary tract infection) and serious adverse event (SAE; surgical site infection, sepsis, post-operative renal failure, venous thromboembolism, cardiac arrest, myocardial infarction, or stroke). The occurrence of any adverse event (AAE) was defined as the occurrence of at least one MAE or SAE. In-hospital morality was separately tabulated.

Statistical analysis

Patient demographic and comorbidity characteristics were compared using chi-squared analysis for categorical data and student's T-tests or ANOVA for continuous data.

Next, 1:1 propensity score matching was performed to addresses potential selection biases in the selection of cohorts, a technique that has been found to be particularly useful when evaluating relatively rare conditions [15]. The CP and non-CP cohorts were matched for age, sex, comorbidity burden, and surgical variables with the PSMATCH2

Table 1
Demographic and comorbid characteristics of aggregate and matched cohorts

	Aggregate Non-CP Cohort		Aggregate CP Cohort		*p-value	Propensity Score Matched Non-CP Cohort§		Propensity Score Matched CP Cohort§		*p-value
	Number	Percent	Number	Percent		Number	Percent	Number	Percent	
Total Patients = 1,518,012	1,513,458	99.70%	4,554	0.30%		4,285	50.00%	4,285	50.00%	
Age	Mean: 55.8 years		Mean: 53.5 years		<0.001	Mean: 55.1 years		Mean: 54.2 years		1.000
< 40	127,968	8.46%	622	13.67%		508	11.86%	503	11.74%	
40-49	345,044	22.80%	1,123	24.67%		1,021	23.84%	1,027	23.96%	
50-59	468,914	30.98%	1,275	28.00%		1,215	28.36%	1,210	28.24%	
60+	571,380	37.75%	1,518	33.33%		1,540	35.94%	1,545	36.06%	
Sex					0.006					1.000
Male	728,949	48.16%	2,429	53.33%		2,229	52.02%	2,219	51.80%	
Female	784,509	51.84%	2,125	46.67%		2,056	47.98%	2,066	48.22%	
Surgical approach					<0.001					1.000
Anterior fusion	1,269,665	83.89%	3,036	66.67%		2,867	66.92%	2,867	66.92%	
Posterior fusion	199,315	13.17%	1,290	28.33%		1,202	28.06%	1,202	28.06%	
Combined anterior-posterior fusion	44,326	2.93%	273	6.00%		215	5.02%	215	5.02%	
Number of operative levels					<0.001					1.000
1	1,005,228	66.42%	2,277	50.00%		2,205	51.46%	2,205	51.46%	
>1	508,230	33.58%	2,277	50.00%		2,080	48.54%	2,080	48.54%	
Elixhauser Comorbidity Index			Median: 0 ECI		<0.001	Median: 0 ECI		Median: 0 ECI		1.000
0	1,154,904	76.31%	2,732	60.00%		2,654	61.94%	2,654	61.94%	
1-5	348,536	23.03%	1,822	40.00%		1,582	36.92%	1,582	36.92%	
6-12	10,019	0.66%	74	1.63%		48	1.12%	48	1.12%	

* = Statistically significant at p < 0.05
§ Matched on age, sex, Elixhauser Comorbidity Index, procedure approach, and multiple operative levels CP = Cerebral Palsy

Table 2

Lengths of hospital stay of aggregate and propensity score matched cohorts

Total Patients = 1,518,012	Aggregate Non-CP Cohort		Aggregate CP Cohort			Propensity Score Matched Non-CP Cohort§		Propensity Score Matched CP Cohort§		
	1,513,458	99.70%	4,554	0.30%		4,285	50.00%	4,285	50.00%	
	Median	IQR	Median	IQR	*p-value	Median	IQR	Median	IQR	*p-value
Length of Stay (days)	1.0	1 - 2	2.0	1 - 4	**<0.001**	2.0	1-3	2.0	1-4	**<0.001**

* Statistically significant at p < 0.05

§ Matched on age, sex, Elixhauser Comorbidity Index, procedure approach, and multiple operative levelsCP = Cerebral Palsy

algorithm. NIS strata and discharge weights were also included in the propensity score matching.

Multiple logistic analyses were used to assess the odds of adverse events in patients with CP as compared to those without CP. These models controlled for age, sex, cumulative ECI, involvement of multiple operative levels, and procedure approach. These analyses were performed for entire cohort and matched cohort populations.

All multiple logistic regression models were constructed on weighted records. The level of significance for all tests was set at p < 0.05. All statistical analyses were performed using STATA version 13 (StataCorp LP, College Station, TX).

Results

Full cohort analyses

After weighting to national estimates, 1,518,012 patients met criteria for inclusion in the study. Of these, 4,554 (0.30%) had CP (Table 1).

On univariate analysis of demographic characteristics, CP patients were younger (mean age of 53.5 years versus mean age of 55.8 years, p < 0.001) and had a higher proportion of males (53.33% versus 48.16%, p = 0.006). The CP cohort had a higher incidence of overall comorbidity burden as evidenced by Elixhauser Comorbidity Index (41.63% of CP patients had one or more comorbidities, compared with 23.69% of non-CP patients; p<0.001).

In terms of surgical approach, CP patients had higher rates of posterior fusion (28.33% versus 13.17%, p < 0.001), and correspondingly lower rates of anterior fusion. Additionally, CP patients had higher rates of multi-level operations (50.00% versus 33.58%, p < 0.001).

Adverse events occurring within the in-hospital postoperative period were then compared between the two patient cohorts (Table 3). CP patients had higher incidences of AAE (6.33% compared with 2.63%, p<0.001) and MAE (5.67% compared with 2.18%, p<0.001).

Multiple logistic regression models controlling for demographic and operative factors were then constructed to determine the odds of postoperative adverse event occurrence in CP cases, with the aggregate non-CP cohort used as the referent. Based on this analysis, there were increased odds of AAE in CP patients (Odds Ratio [OR] = 1.73; 95% CI, 1.30-2.29; p <0.001) and MAE (OR= 1.86; 95% CI, 1.38-2.50; p<0.001). There were no differences in odds of SAE or mortality between the aggregate CP and non-CP cohorts. These results are shown in the right column of Table 3.

Propensity score matched analyses

As a separate analysis to evaluate the robustness of the multiple logistic regression model findings, a non-CP cohort was assembled that was matched to CP cases on the basis of age, sex, comorbidity burden, involvement of multiple operative levels, and procedure approach.

After matching, there were no longer any differences in age, sex, comorbidity burden, involvement of multiple operative levels, nor procedure approach. However, 269 CP cases were unable to be matched to a similar non-CP case, resulting in the matched CP cohort being

smaller than the aggregate CP cohort. The preoperative characteristics and lengths of hospital stay of the matched cohort are included in Table 1 and 2.

Similarly, logistic regression models to determine the odds of adverse events among the propensity matched cohort was performed to further control for patient-specific differences in selected preoperative and operative variables. Statistical significance for odds of AAE (OR= 1.72; 95% CI, 1.05-2.81; p=0.030), and MAE (OR= 2.07; 95% CI, 1.20-3.57; p=0.009) was maintained in the propensity matched analysis. These findings are shown in Table 3 and by forest plot in Figure 1.

Discussion

The recognition that adults with CP are at risk for spinal stenosis has led clinicians in the CP community to increase surveillance and referral for cervical pathology in this population. As myelopathy is often considered for surgical intervention, there is a need to understand the safety of such interventions in this potentially compromised patient population. As such, the current study aimed to characterize the in-hospital odds of complications associated with cervical spinal fusion in cases with CP, compared to cases without CP.

A relatively small percentage of patients undergoing cervical spine surgery had CP (0.30%). This highlights the fact that single institution studies make it difficult to statistically power studies of this population. It was based on this that the NIS database was utilized, as has been done in other spine-related studies.

Patients with CP undergoing cervical fusion were significantly younger and more commonly male than those in a control (non-CP) cohort. The mean age of CP patients undergoing cervical fusion in the present study is 53.8 years. Prior studies have showed a similar age distribution between 45 and 55.3 years [7,11,13,14]. The operative approach of CP and non-CP cases significantly differed. CP cases were more likely to undergo posterior fusion and less likely to undergo anterior fusion than the control group, and had a higher rate of multi-level operations. The higher rate of multilevel surgery may indicate that individuals with CP have more extensive degenerative conditions and cervical stenosis. Additionally, these cases may be more likely to have procedures performed for myelopathy.

Based on multivariate analyses controlling for age, comorbidities, and surgical variables, those with CP were more likely to have minor and any adverse events (ORs of 1.73 and 1.86) than the non-CP referent. The increased incidence of many types of adverse events likely combine to yield a median length of stay that is double that of the non-CP cohort (median: 2.0 vs. 1.0 days). The authors believe the higher risk for these various adverse events stems from the underlying secondary disability caused by progressive cervical spine pathology and speaks to the urgent nature of early diagnosis and treatment.

To control for confounding in a different manner from multiple logistic regression, propensity matching was performed on the basis of demographic, comorbidity, and surgical variables. This represents a distinct statistical methodology from multiple logistic regression and served to test the robustness of the model findings. In the matched models, those with CP had higher odds of minor and any adverse events (ORs of 1.72 and 2.07) than the matched non-CP referent. Importantly, in-hospital

Table 3

Adverse events, returns to operating room, readmissions and mortality by cerebral palsy status

Complication	No Cerebral Palsy (Non-CP)		Cerebral Palsy (CP)		Multivariable Odds Ratio Controlled for Preoperative Variables[†] §Multivariate Propensity Matched Odds Ratio		
Total Patients = 1,518,012	1,513,458	99.70%	4,554	0.30%	OR	95% CI	p-value
Any Adverse Event (AAE)	39,772	2.63%	288	6.33%	**1.73**	**1.30 - 2.29**	**<0.001**
					§ 1.72	1.05-2.81	0.030
Serious Adverse Event (SAE)	10,474	0.69%	39	0.87%	0.82	0.40 - 1.67	0.577
					§ 0.72	0.26-2.01	0.540
Surgical site infection	213	0.01%	0	0.00%			
Sepsis	2,581	0.17%	24	0.53%			
Thromboembolic Events	4,402	0.29%	24	0.53%	'		
Cardiac Arrest	1,670	0.11%	0	0.00%			
MI	1,973	0.13%	0	0.00%			
Stroke	941	0.06%	0	0.00%			
Minor Adverse Event (MAE)	32,941	2.18%	258	5.67%	**1.86**	**1.38 - 2.50**	**<0.001**
					§ 2.07	1.20-3.57	0.009
Pneumonia	9,260	0.61%	90	1.97%			
UTI	17,457	1.15%	147	3.23%			
Renal Failure	8,653	0.57%	39	0.87%			
In-hospital mortality	1,670	0.11%	10	0.22%	1.47	0.36 - 5.96	0.589
					§ 2.10	0.21-20.9	0.527

[†] Preoperative variables controlled for included age, sex, Elixhauser Comorbidity Index, procedure approach, and multiple operative levelsBolding indicates statistical significance at p < 0.05

§ Propensity scores were generated based on age, sex, Elixhauser Comorbidity Index, procedure approach, and multiple operative levels
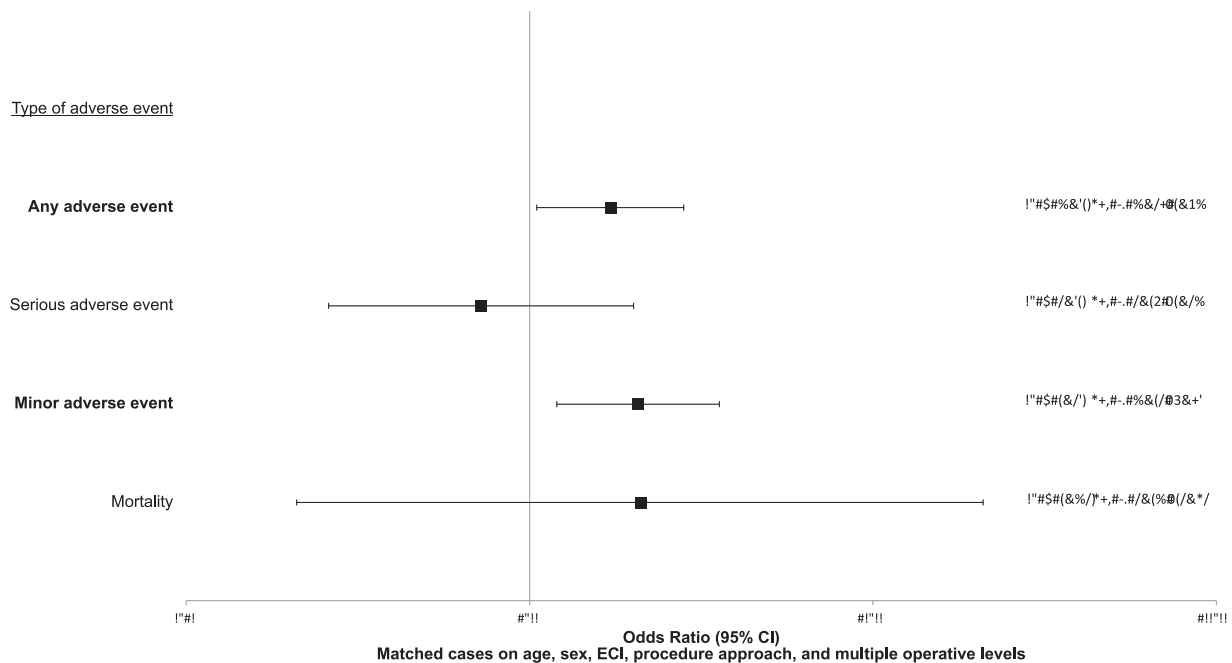

Fig. 1. Propensity score matched odds ratios for in-hospital adverse events after cervical fusion in patients with cerebral palsy

serious adverse events and mortality were not different between the unmatched or matched CP and non-CP cohorts.

Any surgical intervention needs to balance risks and benefits. As more attention is being given to cervical spine conditions in the CP population, more affected patients are being recognized, optimizing the care for this population is clearly important. The present study found that any and minor adverse events (i.e., pneumonia, UTI, and renal failure) occurred at increased rates in the CP group. While this study was not able to detect the precise mechanism for these differences, prior studies have suggested that greater degree of preoperative kyphosis, lack of antifibrinolytic use, increased estimated blood loss, and poor nutrition status may contribute to greater risks of postoperative pulmonary complications and UTI in CP patients [16,17]. Nevertheless, the finding that CP patients experienced in-hospital serious adverse events and mortality at equivalent rates relative to non-CP patients supports the

role for cervical spine surgery in this population. Importantly, medical optimization prior to surgery should be pursued to ensure effective operative outcomes. In addition, an interdisciplinary approach incorporating physical therapists, neurosurgeons, neurologists, physiatrists, and orthopaedic surgeons remains a highly recommended strategy for optimal perioperative management of this medically-complex patient population [18].

There are limitations to the present study that should be noted. Foremost among them is the retrospective nature of the study and potential study group biases that may not have been fully addressed by the propensity score matching and multiple logistic regression analyses. Second, there are intrinsic limitations associated with the administrative data from the National Inpatient Sample; however, this type of dataset was needed to achieve statistical power necessary to evaluate this relatively rare population. Further, the dataset does not delineate between

classifications of CP; geographic, motor types, and functional classes were not available for the study population. Third, decreased overall life expectancy of CP patients relative to the general population could introduce a survivorship bias; however, the propensity score matching employed in the present study served to minimize potential bias by allowing us to compare patients of similar age, sex, and comorbidity burden distributions with versus without CP. Finally, granular surgical data such and post-discharge outcomes were not available in this dataset.

Conclusions

Overall, the current study defined the national CP population undergoing cervical spine surgery. As there is increasing awareness of potentially cervical pathology in the CP population, [8] the findings reported here suggest that surgical intervention for this population can be appropriately considered without severe in-hospital morbidity or mortality. The relative safety of cervical fusion in the CP population with respect to serious adverse events and mortality suggests that, like in the general population, cervical fusion may be utilized in this unique population.

Prepared for submission to

North American Spine Society Journal

Location of Work

Yale School of Medicine, New Haven, CT

Declaration of Competing Interest

J.N.G. has disclosures reported separately.

Funding

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.xnsj.2022.100167.

References

[1] 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.

[2] Odding E, Roebroeck ME, Stam HJ. The epidemiology of cerebral palsy: incidence, impairments and risk factors. Disabil Rehabil 2006;28(4):183–91.

[3] Hirtz D, Thurman DJ, Gwinn-Hardy K, Mohamed M, Chaudhuri AR, Zalutsky R. How common are the "common" neurologic disorders? Neurology 2007;68(5):326–37.

[4] 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(6):509–19.

[5] Patel DR, Neelakantan M, Pandher K, Merrick J. Cerebral palsy in children: a clinical overview. Transl Pediatr 2020;9(Suppl 1):S125–35.

[6] Rice J, Skuza P, Baker F, Russo R, Fehlings D. Identification and measurement of dystonia in cerebral palsy. Dev Med Child Neurol 2017;59(12):1249–55.

[7] Hung CW, Matsumoto H, Ball JR, et al. Symptomatic cervical spinal stenosis in spastic cerebral palsy. Dev Med Child Neurol 2020;62(10):1147–53.

[8] Guettard E, Ricard D, Roze E, et al. Risk factors for spinal cord lesions in dystonic cerebral palsy and generalised dystonia. J Neurol Neurosurg Psychiatry 2012;83(2):159–63.

[9] Anderson WW, Wise BL, Itabashi HH, Jones M. Cervical spondylosis in patients with athetosis. Neurology 1962;12:410–12.

[10] Ebara S, Harada T, Yamazaki Y, et al. Unstable cervical spine in athetoid cerebral palsy. Spine (Phila Pa 1976) 1989;14(11):1154–9.

[11] Harada T, Ebara S, Anwar MM, et al. The cervical spine in athetoid cerebral palsy. A radiological study of 180 patients. J Bone Joint Surg Br 1996;78(4):613–19.

[12] Ebara S, Yamazaki Y, Harada T, et al. Motion analysis of the cervical spine in athetoid cerebral palsy. Extension-flexion motion. Spine (Phila Pa 1976) 1990;15(11):1097–103.

[13] Watanabe K, Otani K, Nikaido T, et al. Surgical outcomes of cervical myelopathy in patients with athetoid cerebral palsy: a 5-year follow-up. Asian Spine J 2017;11(6):928–34.

[14] Azuma S, Seichi A, Ohnishi I, Kawaguchi H, Kitagawa T, Nakamura K. Long-term results of operative treatment for cervical spondylotic myelopathy in patients with athetoid cerebral palsy: an over 10-year follow-up study. Spine (Phila Pa 1976) 2002;27(9):943–8 discussion 948.

[15] Cepeda MS, Boston R, Farrar JT, Strom BL. Comparison of logistic regression versus propensity score when the number of events is low and there are multiple confounders. Am J Epidemiol 2003;158(3):280–7.

[16] Samdani AF, Belin EJ, Bennett JT, Miyanji F, Pahys JM, Shah SA, Newton PO, Betz RR, Cahill PJ, Sponseller PD. Major perioperative complications after spine surgery in patients with cerebral palsy: assessment of risk factors. European Spine J 2016;25(3):795–800.

[17] Tsirikos AI. Development and treatment of spinal deformity in patients with cerebral palsy. Indian J Orthopaedics 2010;44(2):148–58.

[18] Novacheck TF, Gage JR. Orthopedic management of spasticity in cerebral palsy. Child's Nervous System 2007;23(9):1015–31.