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Association Between the Clivus Slope and Patient-Reported Japanese Orthopaedic Association (PRO-JOA) Scores in Patients with Basilar Invagination: A Retrospective Study

Liwei PENG[1], Wei ZUO[1], Chao CHENG[1], Fan YANG[2], Peng WANG[1], Zilong MAO[1], Jin'an ZHANG[1], Weixin LI[1]

[1]Fourth Military Medical University, Tangdu Hospital, Department of Neurosurgery, Xi'an, China
[2]Fourth Military Medical University, Tangdu Hospital, Department of Plastic Surgery and Burns, Xi'an, China

*Liwei Peng, Wei Zuo, Chao Cheng and Fan Yang contributed equally to this work.

Corresponding author: Weixin LI ✉ tangdunaowai@163.com

ABSTRACT

AIM: To determine a quantitative relationship between the postoperative clivus slope (CS) and the change in the Patient-Reported Japanese Orthopaedic Association (PRO-JOA) scores following reduction surgery of the basilar invagination (BI).

MATERIAL and METHODS: A single center retrospective study was conducted. Patients who met the inclusion and exclusion criteria at our hospital during the period from August 2015 to August 2020 were identified. The CS was introduced. Radiographic parameters including the CS were measured to assess realignment preoperatively and postoperatively. The PRO-JOA score was recorded to reveal the clinical outcome. The PRO-JOA score and the radiographic parameters that included the CS were compared between postoperative BI patients.

RESULTS: Ninety-four patients with BI were included in the study. The CS (0.96, 0.93–1.00) was inversely correlated with the PRO-JOA score. The CS was negatively associated with the ΔPRO-JOA score in the crude model, while no significant associations in the fully adjusted model, although in the case of the latter, a slight trend was found (p for trend<< 0.05). In the non-linear model, the CS was negatively associated with the ΔPRO-JOA score in patients diagnosed with BI, unless the CS exceeded 63.4°.

CONCLUSION: A reduction in the CS affects the postoperative PRO-JOA score of BI patients. This relationship can be employed as a quantitative reference in determining preoperative design with respect to the intraoperative correction needed to reduce craniovertebral junction deformity in BI.

KEYWORDS: Clivus slope, Basilar invagination, Craniovertebral junction, Sagittal parameter, Patient-Reported Japanese Orthopaedic Association score

ABBREVIATIONS: PRO-JOA score: Patient-Reported Japanese Orthopaedic Association score, **CS:** Clivus slope, **BI:** Basilar invagination, **AAD:** Atlantoaxial dislocation, **CM:** Chiari malformation, **CVJ:** Craniovertebral junction, **MRI:** Magnetic resonance imaging, **OO:** Os odontoideum, **BMI:** Body mass index, **SVA:** Sagittal vertical axis, **AT:** Axial tilt, **CCT:** Craniocervical tilt, **CXA:** clivoaxial angle, **CMA:** Cervicomedullary angle, **BA:** Basal angle, **BoA:** Boogaard's angle, **HNFA:** Head-neck flexion angle, **OS:** Occipital slope, **CCA:** Craniocervical angle, **SCA:** Spino-cranial angle, **CI:** Cranial incidence, **ADI:** Atlanto-dental interval, **CLV:** Chamberlain's line violation, **STROBE:** Strengthening the reporting of observational studies in epidemiology, **GAM:** Generalized additive model, **NDI:** Neck disability index, **OR:** Odds ratio, **CI:** Confidence interval

Liwei PENG : 0000-0003-0273-7762
Wei ZUO : 0000-0003-0420-1793
Chao CHENG : 0000-0003-2930-5900
Fan YANG : 0000-0002-9595-4290
Peng WANG : 0000-0002-7625-8126
Zilong MAO : 0000-0003-2730-2749
Jin'an ZHANG : 0000-0003-2168-618X
Weixin LI : 0000-0002-7399-8989

INTRODUCTION

Employing the radiographic sagittal parameters from the craniovertebral junction to obtain a better prognosis has become the preferred approach for quantitatively reducing the basilar invagination (BI) (12). However, the relationship between these parameters and the change in the Patient-Reported Japanese Orthopaedic Association (PRO-JOA) score has remained undetermined (16).

BI is caused by occipital dysplasia, which is characterized chiefly by a higher level of the odontoid process than observed in normal patients, extending even to its protrusion into the foramen magnum (2). This can indirectly lead to a shortening of the anteroposterior diameter of the foramen magnum and a narrowing of the posterior cranial fossa, causing a compression of the medulla oblongata and local nerve tracts (5). The condition can be associated with other craniovertebral junction (CVJ) malformations such as platybasia, atlantoaxial dislocation (AAD), Chiari malformation (CM), atlas occipitalization, and Klippel-Feil syndrome (20).

Traditionally, BI is diagnosed based on three sagittal lines, which include Chamberlain's line (the line between the posterior margin of the hard palate and the posterior margin of the foramen magnum), McGregor's line (the line from the posterior margin of the hard palate to the lowest point of the squama occipitalis), and McRae's line (the anteroposterior line of the foramen magnum) (15). BI is also diagnosed from the relationship between the Wackenheim line (the line between the tip of the dorsal saddle and the anterior margin of the foramen magnum) and the odontoid. However, there are few data on the association between the Wackenheim line and clinical outcomes (13). With the ongoing development of radiography, new parameters having diagnostic significance continue to be reported, but the simple angle, clivus slope (CS), has remained unexamined. CS is defined as the angle between the Wackenheim line and the horizonal line.

In this study, we explored whether the CS is associated with PRO-JOA score changes. Based on clinical experience, we hypothesized that CS correction may be significantly associated with changes in the PRO-JOA score, which could be used as a referential index for reducing sagittal deformity in BI.

MATERIAL and METHODS

Study Population

Initially, a total of 289 people who were diagnosed with CVJ malformation between August 2015 and August 2020 at our hospital were screened. All of them had received C1/2 or occipito-cervical internal fixation.

A total of 94 patients were among the final cohort that fell within the following inclusion and exclusion criteria.

Inclusion standards:

1) The distance from the tip of the odontoid to Chamberlain's line ≥ 3 mm;

2) Patients with complete preoperative and postoperative X-ray plain films and magnetic resonance imaging (MRI) materials;

Exclusion standards:

1) patients having only AAD;

2) patients having only Chiari malformation;

3) patients having an odontoideum (OO);

4) patients without internal fixation;

5) patients who underwent revision surgery.

In our study, 289 patients were screened, of which 195 participants were excluded. Among the 195 excluded subjects, 92 were diagnosed with Chiari malformation only, 40 were AAD only, 10 were OO patients, 25 lacked complete imaging data, 8 lacked imaging data, 19 did not receive internal fixation, and 1 received revision surgery, leaving 94 patients for data analysis. The average age of the patients was 39.10 ± 13.21 years, and about 58.51% of the participants were male. The demographics and baseline characteristics are presented in Table I. Details of the selection of cases are presented in Figure 1.

All participants were followed-up with 12 weeks later with at least a telephonic interview. Because the detailed data were collected from the hospital's electronic medical record system, the requirement for written informed consent was waived. The study was approved by the Ethics Committee of our hospital (No. K202011-04).

Measurement of PRO-JOA Score, CS, and Other Covariants

All parameters were measured on cervical radiographs

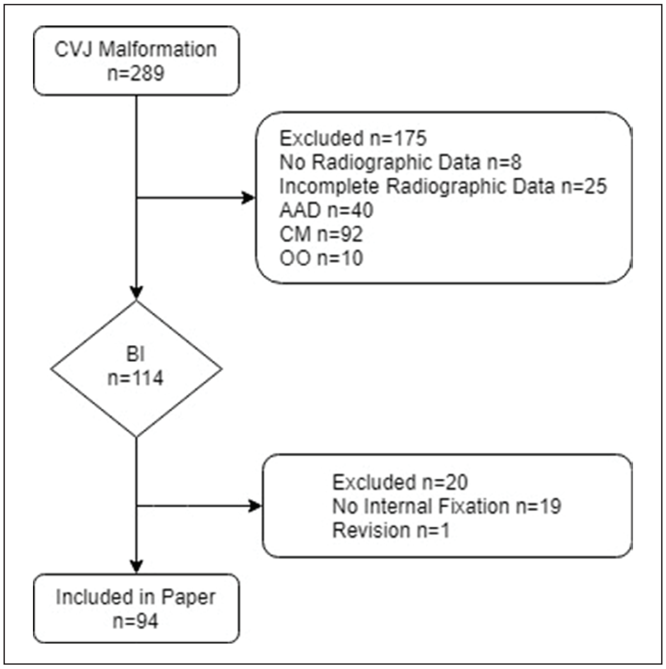

Figure 1: Flowchart of the study.

Table I: Baseline Characteristics of Participants

Characteristic	Q1	Q2	Q3	Q4	p-value	p-value(#)
Number of Patients	21	24	23	23		
Age	39.29 ± 13.09	36.67 ± 14.05	41.96 ± 13.02	39.78 ± 13.36	0.605	0.56
Body Mass Index	23.55 ± 4.18	24.17 ± 4.06	24.67 ± 2.50	24.13 ± 4.48	0.821	0.882
NDI	0.28 ± 0.20	0.23 ± 0.13	0.26 ± 0.20	0.27 ± 0.15	0.813	0.727
CLV	9.35 ± 2.86	9.10 ± 4.82	8.47 ± 5.07	8.79 ± 4.54	0.919	0.483
ADI	2.25 ± 1.27	2.62 ± 1.83	2.11 ± 1.22	2.29 ± 1.45	0.674	0.878
C2-7 SVA	18.09 ± 11.25	15.66 ± 8.31	11.98 ± 8.26	9.73 ± 8.24	**0.021***	**0.018***
C0-1 angle	7.39 ± 7.02	9.23 ± 6.34	9.97 ± 5.43	8.78 ± 4.70	0.536	0.202
C1-2 angle	24.07 ± 10.75	25.08 ± 12.05	22.67 ± 11.74	23.50 ± 11.23	0.909	0.806
C0-2 angle	30.30 ± 11.26	34.02 ± 11.30	32.44 ± 12.78	31.09 ± 13.24	0.746	0.604
C2-7 angle	12.49 ± 11.18	20.86 ± 15.25	22.33 ± 13.89	24.44 ± 11.98	**0.028***	**0.016***
C2 slope	12.55 ± 8.30	8.07 ± 6.21	7.80 ± 6.32	8.08 ± 6.16	0.068	0.132
C7 slope	22.07 ± 9.60	22.69 ± 7.60	22.15 ± 7.18	23.68 ± 10.25	0.933	0.991
Cranial tilt	7.92 ± 6.26	4.99 ± 3.85	5.18 ± 4.26	5.00 ± 2.84	0.11	0.381
Cervical tilt	15.46 ± 9.11	16.34 ± 7.58	20.05 ± 10.19	23.66 ± 7.96	**0.013***	**0.016***
Axial tilt	78.08 ± 12.12	83.90 ± 12.82	85.89 ± 10.99	83.15 ± 9.77	0.15	0.161
Craniocervical tilt	94.00 ± 24.98	103.54 ± 18.43	105.72 ± 23.22	106.43 ± 15.31	0.182	0.291
CXA	118.78 ± 12.68	126.96 ± 11.46	134.06 ± 11.05	144.64 ± 10.08	**<0.001*****	**<0.001*****
CS	33.61 ± 8.04	46.67 ± 2.05	55.59 ± 3.77	70.85 ± 7.58	**<0.001*****	**<0.001*****
CMA	135.70 ± 11.67	144.50 ± 14.63	139.92 ± 10.90	140.57 ± 14.79	0.305	0.193
Basal angle	139.93 ± 9.44	137.04 ± 7.67	128.52 ± 5.92	129.23 ± 11.64	**0.005****	**0.003****
Boogaard's angle	163.63 ± 9.71	164.18 ± 8.53	156.73 ± 10.34	141.87 ± 12.29	**<0.001*****	**<0.001*****
HNFA	78.44 ± 12.66	88.83 ± 13.53	84.41 ± 14.58	90.41 ± 11.17	0.108	0.064
Occipital slope	19.91 ± 12.32	31.29 ± 8.27	30.47 ± 8.68	32.61 ± 8.32	**<0.001*****	**<0.001*****
CCA	62.33 ± 5.79	55.85 ± 7.79	54.92 ± 6.18	56.75 ± 3.86	**0.001****	**0.002****
SCA	85.56 ± 9.02	77.14 ± 7.83	75.25 ± 11.52	73.59 ± 9.36	**0.002****	**0.005****
Cranial incidence	70.77 ± 9.22	71.71 ± 7.76	66.89 ± 7.72	65.53 ± 8.60	0.063	0.15
Sex					0.752	-
Female	12 (57.14%)	12 (50.00%)	14 (60.87%)	15 (65.22%)		
Male	9 (42.86%)	12 (50.00%)	9 (39.13%)	8 (34.78%)		
Posterior cranial nerve symptoms					0.698	-
No	20 (95.24%)	21 (87.50%)	22 (95.65%)	21 (91.30%)		
Yes	1 (4.76%)	3 (12.50%)	1 (4.35%)	2 (8.70%)		
Numbness					0.761	
No	3 (14.29%)	6 (26.09%)	6 (26.09%)	5 (21.74%)		
Yes	18 (85.71%)	17 (73.91%)	17 (73.91%)	18 (78.26%)		
Dizziness					0.678	-
No	11 (52.38%)	11 (47.83%)	13 (56.52%)	15 (65.22%)		
Yes	10 (47.62%)	12 (52.17%)	10 (43.48%)	8 (34.78%)		
BI type					0.282	-
A	14 (66.67%)	19 (79.17%)	12 (52.17%)	15 (65.22%)		
B	7 (33.33%)	5 (20.83%)	11 (47.83%)	8 (34.78%)		
Klippel-Feil syndrome					0.596	-
No	14 (66.67%)	19 (79.17%)	18 (78.26%)	15 (65.22%)		
Yes	7 (33.33%)	5 (20.83%)	5 (21.74%)	8 (34.78%)		

*Values are given in mean ± standart deviation or n(%). **NDI:** Neck Disability Index, **CLV:** Chamberlain's line violation, **ADI:** Atlanto-dental interval, **SVA:** Sagittal vertical axis, **CXA:** Clivo-axial angle, **CS:** Clivus slope, **CMA:** Cervico-medullary angle, **HNFA:** Head-neck flexion angle, **CCA:** Craniocervical angle, **SCA:** Spino-cranial angle.*

with upright position preoperatively and postoperatively. To decrease measuring errors, each figure was recorded using an average value obtained from duplicate measurements. The average value was then determined in a blinded assessment made by two researchers who had not participated in the surgeries in order to reduce subjective potential bias. The researchers then recorded the PRO-JOA score (25).

CS is the angle between the Wackenheim line and the horizontal line, which was introduced by Peng et al. (17). CS is a novel imaging sagittal parameter. The straight line comprising the CS possesses anatomical landmarks that are clearly visible on an X-ray film, facilitating its identification and measurement.

Covariates involved in this present work can be summarized as demographic data, other sagittal parameters, or clinical features. Based on the published guidelines and research, we decided to record the following variables: age, body mass index (BMI), sex, posterior fossa cranial nerve symptoms, numbness, and dizziness.

Other suspected, confounding radiographic parameters included the following angles and distances (Figures 2, 3): C2-7 sagittal vertical axis (SVA) (14); C0-1 angle; C1-2 angle; C0-2 angle; C2-7 angle; C2 slope (18); C7 slope (6); Cervical tilt (24); Cranial tilt (24); Axial tilt (AT) (12); Craniocervical tilt (CCT) (22); Clivo-axial angle (CXA) (11); Cervico-medullary angle (CMA) (3); Basal angle (BA) (4); Boogaard's angle (BoA) (15); Head-neck flexion angle (HNFA) (2); Occipital slope (OS) (26); Craniocervical angle (CCA) (19); Spino-cranial angle (SCA) (9); Cranial incidence (CI) (9); Atlanto-dental interval (ADI); and Chamberlain's line violation (CLV) (1).

All of the above parameters were measured using Surgimap (V2.3.2.1, Nemaris Inc, NY).

Among the different CS groups (quartile, Q1-Q4), the distributions by age, BMI, Neck Disability Index (NDI), CLV, ADI, C0-1 angle, C1-2 angle, C0-2 angle, C2 slope, C7 slope, cranial tilt, axial tilt, CCT, CMA, HNFA, cranial incidence, sex, posterior fossa cranial nerve symptoms, numbness, dizziness, BI type, and Klippel-Feil syndrome were similar. Compared with the Q1 and Q2 groups, participants having higher CS angles had higher C2-7 angles, cervical tilts, and CXA in the Q3 and Q4 groups. By contrast, the Q3 and Q4 groups had lower C2-7 SVAs and SCAs.

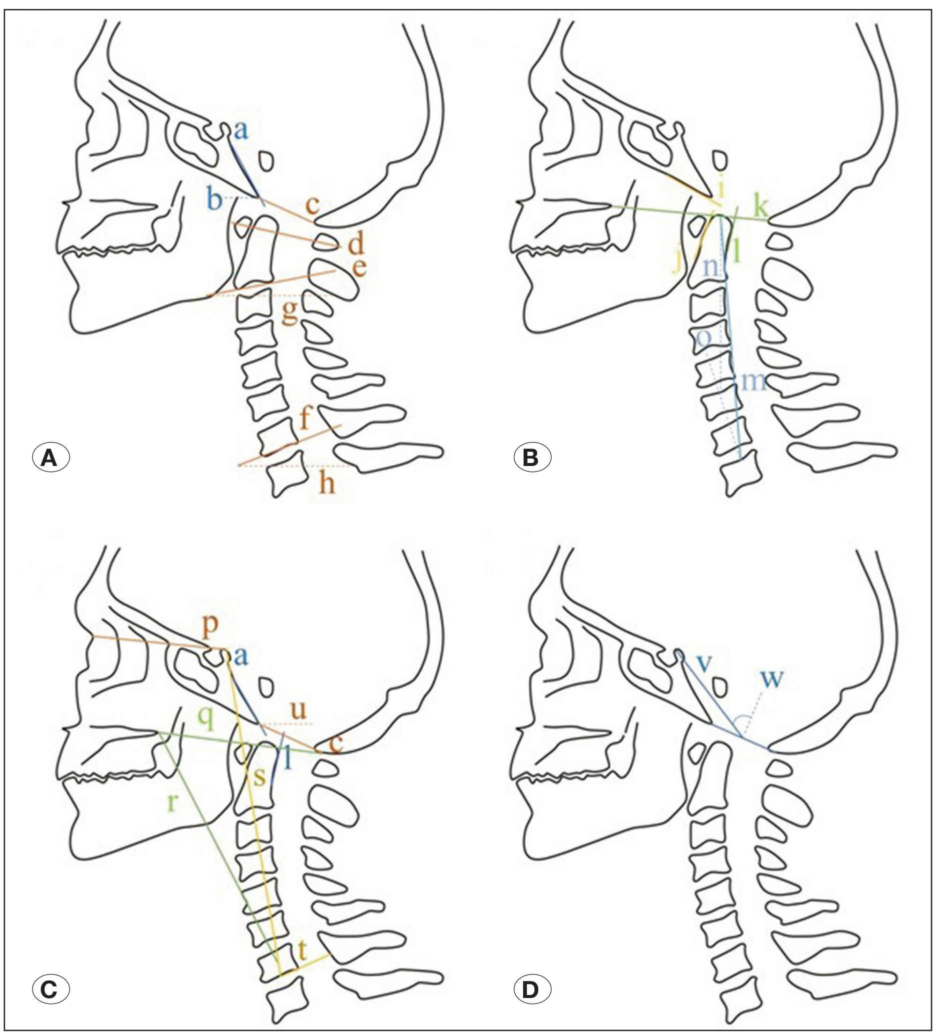

Figure 2: Measurement of craniovertebral and cervical sagittal alignment. **A)** The clivus slope (CS) is subtended between line a and a horizonal line b. The C0-1 angle is subtended between line c and line d, and the C1-2 angle is subtended between line d and line e. The C2-7 angle is subtended between line e and line f. The C2 slope is subtended between line e and the horizonal line g. The C7 slope is subtended between line f and a horizonal line h. **B)** The craniocervical tilt (CCT) is subtended between line i and line j. The axial tilt (AT) is subtended between line k and line l. The cervical tilt is subtended between line m and a vertical line o, and the cranial tilt is subtended between line m and a plumb line n. **C)** The clivo-axial angle (CXA) is subtended between line a and line l. The basal angle (BA) is subtended between line a and line p, and the Boogaard's angle (BoA) is subtended between line a and line c. The head-neck flexion angle (HNFA) is subtended between line p and line l, and the occipital slope (OS) is subtended between line c and a horizonal line u. The craniocervical angle (CCA) is subtended between line q and line r, and the spino-cranial angle (SCA) is subtended between line s and line t. **D)** Cranial incidence (CI) is subtended between line v and line w.

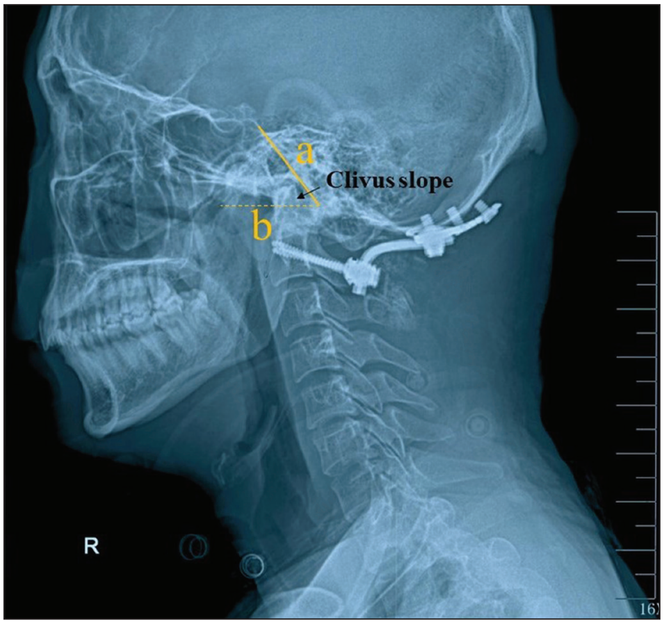

Figure 3: Postoperative lateral radiographies of a basilar invagination (BI). The clivus slope (CS) is subtended between line a and a horizonal line b of the BI case.

Statistical Analysis

First, continuous variables were expressed as the mean ± standard deviation (normal distribution) or the median (quartile; skewed distribution), and categorical variables were expressed as a percentage (%). The chi-square tests (categorical variables), one-way ANOVA (normal distribution), and Kruscal-Whallis H test (skewed distribution) were used to test for statistical differences between the baseline data of each group pair.

Second, we employed univariate, linear regression models to determine the association between the CS and ΔPRO-JOA scores. Third, based on the STROBE statement (21), three models, which included the unadjusted, minimally adjusted, and fully adjusted data, were listed in the paper simultaneously. The adjusted covariances were required to comply with the following criterion, namely, that they caused at least a 10% change in the matched odds ratio (8). Fourth, a generalized additive model (GAM), a method used to identify non-linear relationships, was employed in the present study. If a non-linear association was observed, the threshold effect of CS on the ΔPRO-JOA score was then calculated using a two-piecewise linear regression model. When the ratio of ΔPRO-JOA score to CS in the smooth curve was easily discerned, the recursive method used the maximum model likelihood to automatically calculate the inflection point (10). Fifth, we performed subgroup analyses using stratified linear regression models. The modification and interaction of subgroups were inspected by the likelihood ratio test. Sixth, sensitivity analyses were listed as follows. To increase the robustness of the data analysis, we converted CS into a categorical variable as quartiles and calculated the p value for trends. The aim here was to validate the CS results as a continuous variable, and then to inquire whether there existed a nonlinear relation between the CS and ΔPRO-JOA scores.

All analyses were performed by the statistical software packages R (http://www.R-project.org, The R Foundation) and EmpowerStats (http://www.empowerstats.com, X&Y Solutions, Inc., Boston, MA). P values less than 0.05 (two-sided test) were considered to be statistically significant.

RESULTS

Univariate analysis

The results of the univariate analysis demonstrated that Boogaard's angle (1.04, 1.00–1.08) was positively correlated with the ΔPRO-JOA score. By contrast, we found that age (0.95, 0.91–0.98), NDI (0.01, 0.00–0.79), CXA (0.96, 0.92–0.99), CS (0.96, 0.93–1.00), and HNFA (0.94, 0.88–1.00) were correlated with poor outcome of the ΔPRO-JOA score (Table II).

Multivariate Analysis

We explored the linearity of the association between the CS and ΔPRO-JOA score and the robustness of our results using the unadjusted and adjusted models Table III. In the crude model, we found that CS was inversely associated with the ΔPRO-JOA score [odds ratio (OR): 0.96, 95% confidence interval (CI): 0.93–1.00, p=0.0289]. We observed that a unit increase of CS was associated with a 4% reduction in the ΔPRO-JOA score. In the minimally adjusted model (adjusted age, sex), we did not see obvious changes (OR: 0.96, 95% CI: 0.92–0.99, p=0.0172). This meant that for every 1 unit increase in CS, the ΔPRO-JOA score was reduced by 4%. In the fully adjusted model (OR: 0.94, 95% CI: 0.87–1.01), there was no statistical significance between the CS and the ΔPRO-JOA score. In order to conduct sensitivity analysis, we converted the CS into a categorical variable (quarter). This conversion generated a different trend (p for the trend was <0.05), which indicated that the CS could be used as an exposure factor to characterize its relationship with the ΔPRO-JOA score.

The Analyses of Non-Linear Relationship

Using the GAM and recursive algorithm, we obtained an inflection point located at 63.4°. When the CS < 63.4°, an increase in 1 unit of CS was associated with a 14% decrease in the ΔPRO-JOA score (adjusted OR: 0.86, 95% CI: 0.77, 0.97). However, we failed to observe an association between CS and the ΔPRO-JOA score (OR= 1.11, 95% CI: 0.95, 1.31) on the right side of the inflection point (Table IV).

This result showed that CS was negatively associated with the ΔPRO-JOA score in patients diagnosed with BI, unless the CS exceeded 63.4°. This result also indicated that there was a saturation effect in this region in the relationship between CS and the ΔPRO-JOA score (Figure 4).

Subgroup Analysis

As shown in Figure 5, the tests for parameter interactions were not statistically significant for age, sex, BMI, posterior fossa cranial nerve symptoms, BI type, and Klippel-Feil

Table II: Univariate Analysis of the Crude Association Between ΔPRO-JOA Score and CS

	Statistics	OR (95%CI)	p-value
Age	39.10 ± 13.21	0.95 (0.91, 0.98)	**0.005****
Sex			
Female	55 (58.51%)	1	
Male	39 (41.49%)	0.77 (0.31, 1.91)	0.5708
Height	152.21 ± 27.60	0.99 (0.98, 1.01)	0.4183
Weight	59.30 ± 12.88	0.97 (0.94, 1.01)	0.1072
BMI	24.13 ± 3.80	0.95 (0.84, 1.08)	0.4304
NDI	0.26 ± 0.17	0.01 (0.00, 0.79)	**0.0382***
Posterior cranial nerve symptoms			
No	87 (92.55%)	1	
Yes	7 (7.45%)	2.42 (0.28, 21.13)	0.4243
Numbness			
No	21 (22.58%)	1	
Yes	72 (77.42%)	0.53 (0.16, 1.77)	0.3062
Dizziness			
No	52 (55.91%)	1	
Yes	41 (44.09%)	1.38 (0.55, 3.47)	0.4969
BI type			
A	63 (67.02%)	1	
B	31 (32.98%)	0.45 (0.18, 1.15)	0.0965
Klipper-Feil syndrome			
No	68 (72.34%)	1	
Yes	26 (27.66%)	1.39 (0.49, 3.97)	0.5401
CLV	8.92 ± 4.38	1.00 (0.90, 1.11)	0.9781
ADI	2.32 ± 1.44	1.00 (0.73, 1.36)	0.9783
C2-7 SVA	14.10 ± 9.48	1.01 (0.96, 1.06)	0.7492
C0-1 angle	8.90 ± 5.87	1.02 (0.94, 1.10)	0.6582
C1-2 angle	24.01 ± 11.39	1.02 (0.98, 1.07)	0.2757
C0-2 angle	32.14 ± 12.01	1.02 (0.98, 1.06)	0.298
C2-7 angle	19.85 ± 13.71	1.01 (0.97, 1.04)	0.713
C2 slope	9.24 ± 6.93	1.00 (0.94, 1.07)	0.996
C7 slope	22.64 ± 8.50	1.03 (0.97, 1.09)	0.3596
Cranial tilt	5.79 ± 4.53	0.95 (0.86, 1.06)	0.3709
Cervical tilt	18.74 ± 9.07	0.99 (0.94, 1.05)	0.8292
Axial tilt	82.87 ± 11.64	0.98 (0.94, 1.02)	0.2665
Craniocervical tilt	102.99 ± 20.91	0.99 (0.97, 1.01)	0.3523
CXA	131.20 ± 14.47	0.96 (0.92, 0.99)	**0.0159***
CS	52.02 ± 14.61	0.96 (0.93, 1.00)	**0.0289***
CMA	140.40 ± 13.37	1.02 (0.98, 1.06)	0.4252
Basal angle	134.58 ± 9.74	1.07 (0.99, 1.14)	0.0743
Boogaard's angle	156.75 ± 13.49	1.04 (1.00, 1.08)	**0.0262***
HNFA	85.62 ± 13.54	0.94 (0.88, 1.00)	**0.0351***
Occipital slope	28.79 ± 10.37	0.99 (0.95, 1.04)	0.8001
CCA	57.50 ± 6.61	1.02 (0.95, 1.10)	0.5699
SCA	77.87 ± 10.22	1.01 (0.96, 1.07)	0.5786
Cranial incidence	68.94 ± 8.53	1.04 (0.98, 1.10)	0.2199

Table III: Relationship Between CS and ΔPRO-JOA Score in Different Models

Variable	Crude model OR (95%CI)	p-value	Minimally adjusted model OR (95% CI)	p-value	Fully adjusted model OR (95% CI)	p-value
CS	0.96 (0.93, 1.00)	**0.0289**	0.96 (0.92, 0.99)	0.0172	0.94 (0.87, 1.01)	0.1115
CS (quartile)						
Q1	Referent		Referent		Referent	
Q2	1.17 (0.21, 6.51)	0.8605	1.24 (0.20, 7.61)	0.8125	1.80 (0.12, 26.26)	0.6672
Q3	0.18 (0.04, 0.79)	**0.0231**	0.18 (0.04, 0.82)	**0.0268**	0.10 (0.01, 1.74)	0.1152
Q4	0.26 (0.06, 1.14)	0.0741	0.22 (0.05, 1.05)	0.0584	0.11 (0.01, 1.42)	0.0904
P for Trend	0.0121		0.0111		0.0264	
Crude model: adjusted no covariants						
Minimally adjusted model: adjusted for age and sex						
Fully adjusted model: adjusted for Age; Sex; CLV; ADI; C2-7 SVA; C0-1 angle; Cranial tilt; CMA; CCA; SCA						

***CI:** Confidence interval.*

Table IV: Threshold Effect and Saturation Effect Analysis of CS on ΔPRO-JOA Score Using Piece-wise Linear Regression

Inflection point of CS	Crude OR (95%CI)	p-value	Adjusted OR (95%CI)	p-value
<63.4	0.94 (0.89, 0.99)	0.0201	0.86 (0.77, 0.97)	**0.0133**
≥63.4	1.03 (0.93, 1.13)	0.6195	1.11 (0.95, 1.31)	0.1963
Adjusted model: adjusted for Age; Sex; CLV; ADI; C2-7 SVA; C0-1 angle; Cranial tilt; CMA; CCA; SCA				

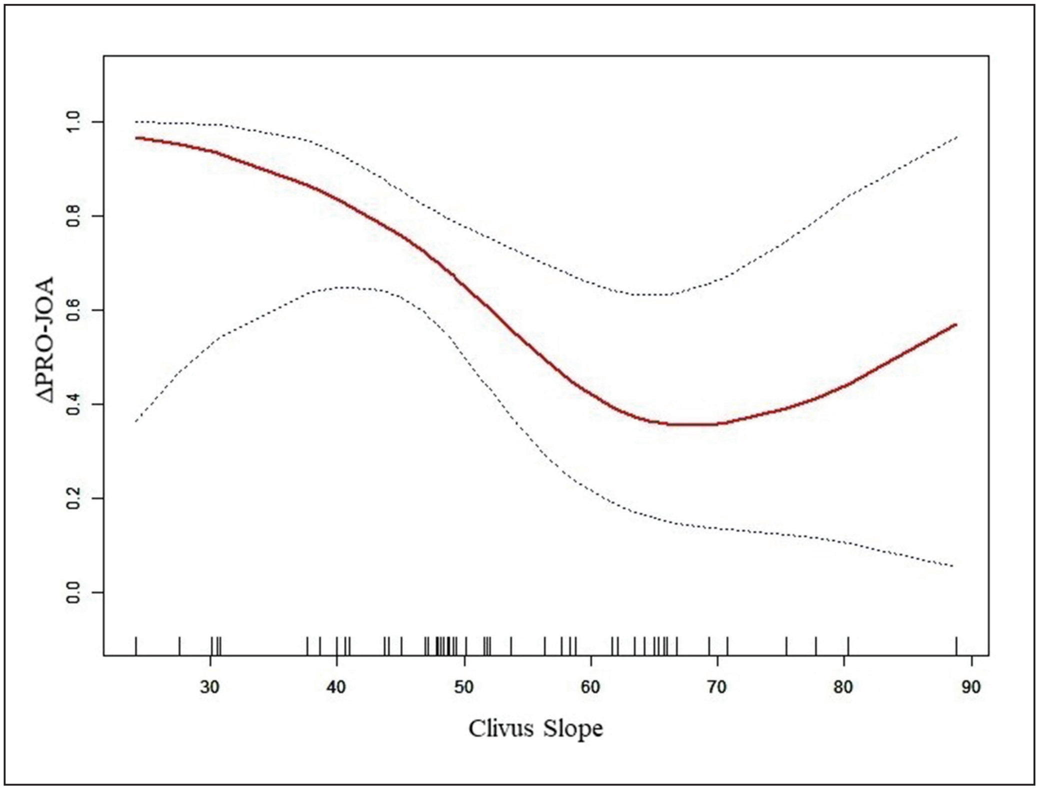

Figure 4: Association between the Patient-Reported Japanese Orthopaedic Association (PRO-JOA) score and clivus slope (CS). The inflection point of CS was 63.4°.

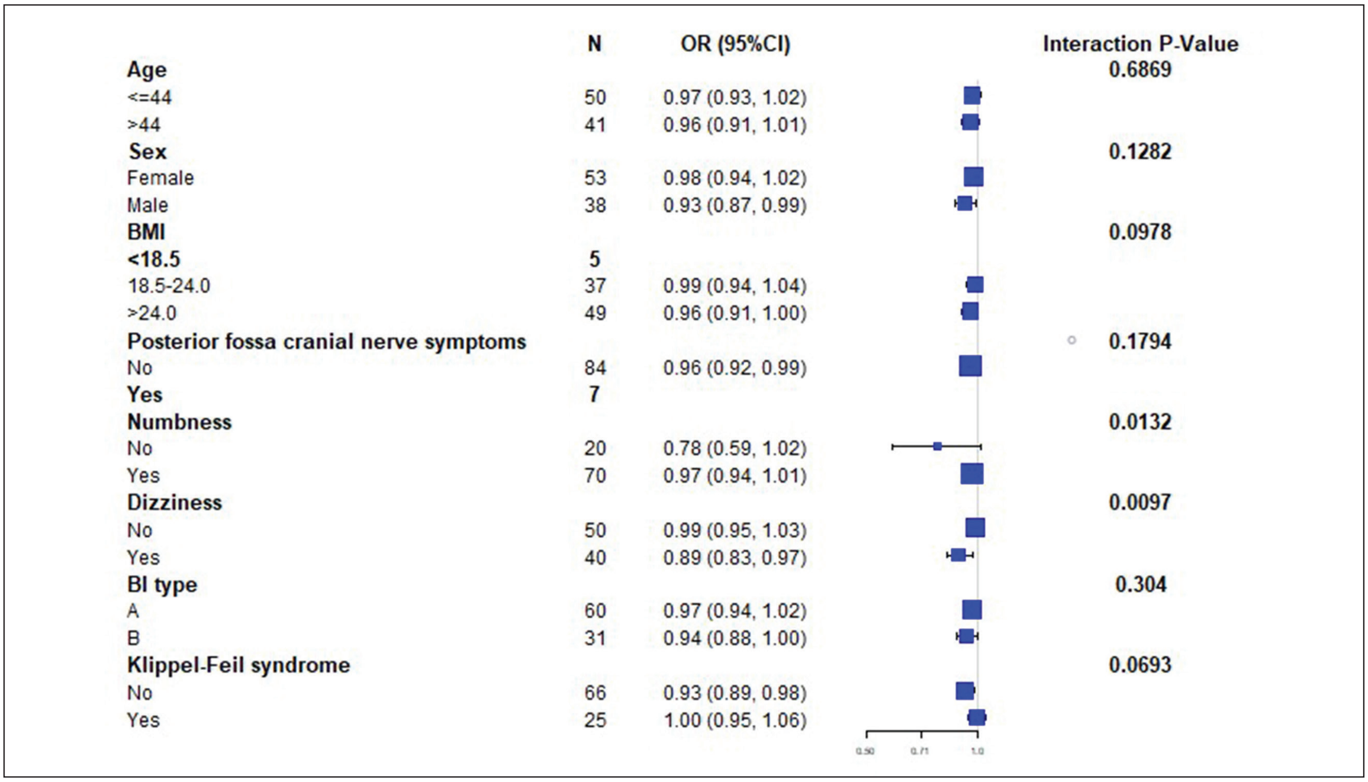

Figure 5: Effect size of clivus slope (CS) on the Patient-Reported Japanese Orthopaedic Association (PRO-JOA) score in pre-specified and exploratory subgroups.

syndrome, while the tests for interactions were significant for parameters reflecting numbness and dizziness. Additionally, we found that the association of CS with the ΔPRO-JOA score was only significant in participants displaying dizziness. In patients with dizziness symptoms, a difference of 1 unit in the CS was associated with an 11% difference in the ΔPRO-JOA score (95% CI: 0.83–0.97). We also found a negative association between the CS and ΔPRO-JOA score in people having numbness.

DISCUSSION

This study aimed to investigate whether CS was independent of the ΔPRO-JOA score. Given that the PRO-JOA score is associated with a prognosis of BI, a determination of this score is significant. In the present study, we found that CS and ΔPRO-JOA were independent after accounting for age, BMI, CLV, ADI, C2-7 SVA, C0-1 angle, Cranial tilt, CMA, CCA, and SCA. However, a non-linear relationship between the CS and ΔPRO-JOA score was observed. The significance of this association was limited to the left side of the inflection point, whereas the association on the right side was not statistically significant. It is worth noting that a negative association with the ΔPRO-JOA score was found in participants with dizziness.

CLV is the most widely used indicator in the diagnosis of BI, with a value of CLV ≥ 3 mm currently defining BI (7). However, in clinical practice, indicators and parameters related to clinical manifestations and patient prognosis are preferred (25). The CS is modified from the CPA (13). The CPA is the angle between the Wackenheim line and the tangent line of the hard palate plane. Based on clinical experience, the CPA cannot be adjusted intraoperatively. If the imaging sagittal parameters do not change before and after surgery, then their diagnostic significance is questionable. It is not appropriate to generate the CPA solely to simplify the CXA and CDA to provide for possible diagnostic significance in imaging (23). Instead, the clinical significance of the parameters should be considered. The CPA cannot reflect a ventral compression of the odontoid process on the brainstem and medulla oblongata. Therefore, a correction based on the CPA is recommended. This association includes the CS.

CS is not affected by factors such as congenital malformations or natural degeneration, unlike the CXA (13). Compared with the CPA, the CS is easier to measure, and can be adjusted intraoperatively. The determination of the association between CS and clinical scores such as the PRO-JOA can help guide reductive surgery, making the surgical goal more targeted. The CS can be considered as a significant outcome predictor, and it can be used to correct sagittal malalignment quantitatively based on imaging data to achieve an ideal sagittal alignment for the patient.

The present study has several strengths. First, both the generalized linear model and GAM clarified the relationship between the CS and ΔPRO-JOA score. Specifically, the GAM is proficient in addressing non-linear relations; it can accommodate non-parametric smoothing, and it enables the fitting of a regression spline to the data. Second, the exposure variable (CS) was handled as both a continuous variable and a categorical variable, minimizing contingency on the data analysis. Third, we found an inflection point for the saturation effect between the CS and ΔPRO-JOA score, which can be informative to the clinician involved in making medical decisions. Fourth, the subgroup analysis increased the robustness of the study. The negative association of CS with the ΔPRO-JOA score in subjects with dizziness was also discovered in the subgroup analysis. Finally, we measured and analyzed 23 sagittal radiographic parameters to account for confounding factors related to the CS and ΔPRO-JOA, which somewhat avoided the selection bias.

This study has several limitations. First, the study was a retrospective analysis and so provided only weak evidence of an association between the CS and ΔPRO-JOA score. Therefore, determining causal relationships is not possible, and experimental study designs will be needed to address this issue. Second, this paper focused on the association between the CS and ΔPRO-JOA score, but did not take the predictive value of CS into consideration. In the future, a predictive model will be developed and validated, incorporating CS as a potential predictor parameter. Third, owing to the fact that the study population contained only Chinese subjects, it may not be generalizable to other ethnic groups.

CONCLUSION

In this study, we observed that correction of the CS influences the postoperative PRO-JOA score of BI patients. The relationship between the CS and ΔPRO-JOA score is non-linear. The CS is negatively related with the ΔPRO-JOA score when the CS is less than 63.4°. This relationship can offer a quantitative reference for the preoperative design and the intraoperative correction so as to reduce CVJ deformity in BI.

AUTHORSHIP CONTRIBUTION

Study conception and design: LP, WZ, WL
Data collection: LP
Analysis and interpretation of results: LP, FY
Draft manuscript preparation: LP, FY
Critical revision of the article: CC, WL
Other (study supervision, fundings, materials, etc...): PW, JZ, ZM
All authors (LP, WZ, CC, FY, PW, ZM, JZ, WL) reviewed the results and approved the final version of the manuscript.

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