Original Article

EuroQol-5 dimensions health-related quality of life questionnaire in craniovertebral instability treated with posterior fixation with or without occipital plating: A comparative study with matched datasets

ABSTRACT

Objective: Health-related quality of life (HRQoL) in craniocervical instability (CCI) before and after posterior fixation is yet to be determined. This study aimed to deliver novel and clinically relevant data about HRQoL (baseline, at follow-up, predictors, and correlates) in subjects with CCI treated with posterior fixation with or without occipital plating, and to compare it with matched datasets.

Methods: EuroQol-5 dimensions (EQ-5D) questionnaires were collected to evaluate HRQoL before surgery and at follow-up. Study sample size was estimated at 58. Comparison with representative datasets was done by matching on a many-to-many basis. Classic CCI parameters were measured. Strengthening the Reporting of Observational Studies in Epidemiology was followed.

Results: Sixty subjects were included. The mean age was 37.2 years. The median follow-up for EQ-5D was 26.3 months with interquartile range (IQR) 10.8 to 47.3 months. The median preoperative score of the 3-level version of EQ-5D (EQ-5D-3L) was 0.254 (IQR = -0.025 to 0.504), whereas at follow-up, it increased to 0.779 (IQR = 0.387–0.864) which is still worse than the 25th percentile (0.894) of the age-matched population. Occipital plating ($n = 35$; 58.3%) did not influence HRQoL trajectory ($P = 0.692$). In multiple linear regression, HRQoL at follow-up was affected by the age ($\beta = -0.004$; $P = 0.049$) and length of hospitalization ($\beta = -0.134$; $P = 0.010$). Of radiologic measurements, preoperative Wackenheim line correlated with HRQoL at follow-up (rho = -0.432; $P = 0 - 028$).

Conclusions: HRQoL is significantly reduced in CCI. Although this can be improved with posterior fixation, it is still worse than the age-matched population. Occipital plating may not influence HRQoL. HRQoL of the elderly might not increase as much as of the younger subjects. The longer hospitalization, the worse HRQoL could be expected. Preoperative Wackenheim parameter could correlate with HRQoL at follow-up.

Keywords: Atlantoaxial fusion, atlantooccipital fusion, craniocervical fixation, EuroQol-5 dimensions-3L, health-related quality of life, occipital plating

INTRODUCTION

Craniovertebral junction is a durable complex of articulations and ligaments.[1] Its instability, however, is potentially lethal due to vicinity of the critical neurovascular structures.[2-4] If the prehospital stage is survived, it oftentimes requires reduction and instrumentation. In recent years, the most popular technique of CCJ stabilization has been C1 lateral mass-C2 pedicle screw fixation with bicortical purchase.[3] This procedure was first introduced by Atul Goel in 1994 and then further developed by Harms in 2001.[5,6] CCJ dislocation and instability are understood to affect patients' health-related

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quality of life (HRQoL),[7,8] but the quantification of this phenomenon is yet to be determined. Moreover, HRQoL after craniocervical fusion is also unknown.

Therefore, we aim to present the first study of both adults and pediatrics, which shall detect the baseline HRQoL before craniocervical fusion and at follow-up. Furthermore, since it has been a matter of debate whether inclusion of the occiput is necessary for the craniovertebral stabilization,[9] we decided to conduct a direct comparison (HRQoL in groups with versus without the occipital plating) to aid the debate. The secondary goal was to determine whether there are any clinical or radiologic predictors of the follow-up HRQoL, and to compare the results with comorbidity-matched and age-matched datasets.

METHODS

Study design

It is an observational study whose concept has been reviewed and approved by the Institutional Review Board (KB-0012/24/04/2020/Z). Patients undergoing posterior craniocervical junction fusion at the tertiary neurosurgical center due to CCI were reviewed for eligibility criteria. EuroQol-5 dimensions (EQ-5D) questionnaires were collected to determine HRQoL prior to surgery and at follow-up via structured phone interview or directly during an outpatient visit. Strengthening the Reporting of Observational Studies in Epidemiology checklist was followed to provide a structure of quality.

Sample size estimation

Pwr package in RStudio was used for the sample size calculation with "pwr.f2.test" function. Based on the background information from similar studies on HRQoL in rare cervical spine entities,[10,11] the effect size was set at 0.35. Accepting probability of type I error at 5% ($\alpha = 0.05$) and expecting type II error at 20% ($\beta = 0.2$) with theoretical power of the study set at typical 80%, and a possible dropout rate at 30%, the minimum sample size has been estimated at 57,149 subjects (rounded up to 58) in the study group for significance of the multiple linear regression model with one dependent and four independent predictor variables.

Patient selection

Eligibility was met if (1) a subject suffered from CCI, (2) CCI was treated with instrumentation using posterior approach, (3) C1-C2 segment was included in fusion (additional inclusion of the occiput and/or lower cervical spine were acceptable, and discrete analysis was planned in advance for those with the occiput plating), and (4) cause of CCJ dislocation or instability was known. Radiologic evaluation was addressed if both preoperative and postoperative computed tomography scans of sufficient quality were accessible. HRQoL was calculated if follow-up was available. Patients were excluded from the study if (1) CCI was treated conservatively without posterior instrumentation, (2) patients could not comprehend the meaning of the questionnaire, (3) CT scans were of poor quality and, therefore, not able to be reformatted into sagittal sections, and (4) there was prior instrumentation of the craniocervical junction. The control group for age-matching on a many-to-many basis was obtained from the representative national database published by Golicki et al.[12,13]

Data extraction

The following items were extracted: (1) age at the time of surgery, (2) sex, (3) date of the follow-up, (4) cause of craniocervical dislocation, (5) symptomatology upon admission and (6) upon discharge, (7) level of instrumentation, (8) hardware system, (9) occipital involvement in fusion, (10) telephone number, (11) blood loss (mL), (12) duration of the surgery (minutes), and (13) duration of the entire hospitalization (days).

Surgical procedure

Every patient was subject to C1-C2 fixation via lateral masses of C1 and pedicles of C2. Adjacent levels were fixed with respect to medical indications. The procedure was carried out using either SUMMIT® SI OCT Spinal Fixation System Instruments (DePuy Synthes, USA; $n = 54$) or Synapse™ OCT system (DePuy Synthes, USA; $n = 6$). Skin incision was linear and muscular stage was performed in a standard manner.[14] Occipital plating was done if gross atlanto-occipital instability was present and for Type A basilar invagination of Goel's classification[15] with separate analysis for each group (with occipital plating versus without). Additional small maneuvers such as C1 laminectomy or reduction of the dislocation were done as necessary for relevant pathologies.

Quality of life assessment

Subjects or their caregivers were communicated with and the questionnaire was presented to them. EQ-5D-3L Paper Telephone v2.0 (ID 71378) and EQ-5D-Y Paper Proxy1 v1.0 (ID 54602) were used (EuroQol Group, Rotterdam, The Netherlands). Preoperative quality of life was assessed as well as the quality on the day of the follow-up. EQ-5D is a tool commonly used in spine surgery evaluating HRQoL.[16,17] It assesses five domains: (1) mobility, (2) self-care, (3) usual activities, (4) pain/discomfort, and (5) anxiety/depression. The score is obtained in the form of a five-digit number that depicts the patient's health state. This five-digit number is then transformed into measurable and convenient utility by means of the standardized chart.[12] Results range from −1 to 1. 0 is equal to death and 1 is equal to perfect health. Negative

values are interpreted as HRQoL that is worse than death as perceived by a given individual. In addition, patients were also asked to depict their HRQoL in a scale from 0 (worst imaginable health state) to 100 (best imaginable health state). Finally, following methods described elsewhere,[10] EQ-5D values were compared with the HRQoL of the age-matched representatives from the national database in Poland[12,13] so as to determine the size of a potential gap between the CCJ subjects following surgery and the general population. Another matching was performed for comorbidities so as to visualize the difference between HRQoL of patients with CCI and of those with similar conditions without CCI. Both matchings were conducted on a many-to-many basis.

Software and measurements

By means of OsiriX MD 11.0 (Pixmeo SARL, Bernex, Switzerland), the following items were measured by two observers (a neurosurgical resident and neurosurgeon): (1) atlanto-dental interval, (2) revised condyle-C1 interval, (3) dens to McRae line, (4) dens to Chamberlain line,[5] dens to McGregor line, (6) dens to Wackenheim, (7) basion-axial interval, (8) basion-dental interval, (9) C2 isthmus height and internal height to determine if HRVA is present, (10) Powers ratio, (11) sagittal diameter of spinal canal at the level of C1 and foramen magnum, and (12) C2 pedicle width to detect narrow pedicles. Normal limits were retrieved from the studies of Kanodia *et al.*, Pawar *et al.*, Ulbrich *et al.*, Dahdaleh *et al.*, and Marathe *et al.*[18-22] Prevalence of high-riding vertebral arteries (isthmus height ≤5 mm or/and C2 internal height ≤2 mm) and narrow pedicles (C2 pedicle width <4 mm) was determined only in adults since pediatric norms have not been established.[23,24] Every measured parameter was included in the correlation analysis. For significant measurements in correlation analysis, inter-software and inter-observer agreement coefficients were analyzed to determine reproducibility. Inter-software reliability between the primary software (OsiriX MD) and RadiAnt DICOM Viewer version 2020.2 (Medixant, Poznan, Poland) was acknowledged by kappa statistic ranging from −1 to 1, with 0 equal to randomness, and 1 indicating perfect reproducibility. As widely accepted, the kappa values were interpreted as: <0.20 poor reliability, 0.21–0.40 fair, 0.41–0.60 moderate, 0.61–0.80 good, and >0.80 excellent reliability. To increase reliability, the observers obtained a standardized instruction in PowerPoint slideshow (Microsoft, Redmond, USA) delineating measurements, finalized with measuring ten nonrelated cases, question-and-answer session, and debriefing.

Statistical analysis

Statistical analysis was performed by means of RStudio version 1.3.1093 (Boston, Massachusetts, USA) and Statistica 13.3.0, TIBCO Software Inc. (Palo Alto, California, USA) by TK.

Medians were supplemented with corresponding interquartile ranges (IQRs) whereas means with standard deviations (SD). For testing a null hypothesis of equal medians with regard to pre- and postoperative nonparametric outcomes, a Wilcoxon test was used. Spearman's rank correlation rho was estimated for each classic radiologic measurement and the follow-up HRQoL. Multiple linear regression analysis was conducted to determine factors correlating with an outcome of interest at follow-up. A linear adaptation of the HRQoL trajectory based on multiple regression was created in RStudio with ggPredict().

RESULTS

Cohort characteristics

The subject characteristics are presented in Table 1. Of sixty subjects who underwent posterior craniocervical instrumentation between 2006 and 2021, thirty were

Table 1: Study group characteristics

Feature	Value
Sex (%)	
Female	30 (50.0)
Male	30 (50.0)
Age (years)	37.2±26.5
CCI cause (%)	
Traumatic	24 (40.0)
Congenital	16 (26.7)
Rheumatic	12 (20.0)
Tumor	6 (10.0)
Grisel syndrome	1 (1.7)
Levels of instrumentation (%)	
O-C1-C2	18 (30.0)
O-C1-C2-C3	10 (16.7)
C1-C2	16 (26.7)
C1-C2-C3	9 (15.0)
Others	7 (11.7)
Duration of surgery (min)	224 (IQR 170-268.8)
Blood loss (mL)	320 (IQR 200-500)
Age >18	415 (IQR 300-537.5)
Age <18	200 (IQR 100-325)
Hospital stay (days)	10 (IQR 9-17)
HRQoL (EQ-5D-3L summary index)	
Total preoperative	0.254 (IQR=-0.025-0.504)
Total at follow-up	0.779 (IQR=0.387-0.864)
Age >18 preoperative	0.224 (IQR 0.090-0.390)
Age >18 follow-up	0.739 (IQR 0.275-0.868)
Age <18 preoperative	0.284 (IQR-0.176-0.716)
Age <18 at follow-up	0.814 (IQR 0.462-0.853)
Neurological status (%)	
Myelopathy preoperative	41 (68.3)
Improved postoperative	22 (53.7)
Stable postoperative	16 (39.0)
Deteriorated postoperative	3 (7.3)

CCI: Craniocervical instability, HRQoL: Health-related quality of life, IQR: Interquartile range

females (50%) and thirty were males (50%). The mean age of the group at the time of operation was 37.2 years (SD = 26.5). The median time from the procedure until the last follow-up was 26.3 months (IQR = 10.8–47.3). The most common cause of CCI was trauma (n = 24; 40%). Of traumatic patients, falls (n = 11; 45.9%) and motor vehicle accidents (n = 7; 29.2%) prevailed. The most common type of CCI was atlantoaxial instability (n = 38; 63.3%), followed by combined atlantoaxial and atlantooccipital instabilities (n = 12; 20.0%). Pure atlantooccipital dislocation was observed in eight subjects (13.3%). In two cases, it was undetermined. Neurological deficits due to spinal cord compression (myelopathy) were present preoperatively in 71.4%. The most common levels of instrumentation were as follows: O-C1-C2 in 18 cases (30.0%) and C1-C2 in 16 cases (26.7%). The occiput was plated in 35 subjects (58.3%). The median duration of the surgery was 224 min (IQR = 170–268.8). The median blood loss in the entire cohort was 320 ml (IQR = 200-500). Unsurprisingly, the median blood loss was higher in adults than in those under 18 years old (415 ml and 200 ml, respectively). The median hospital stay was 10 days (IQR = 9–17).

Quality of life evaluation

The median timing of the second questionnaire was 26.3 months after surgery (IQR = 10.8–47.3). The median preoperative EQ-5D was 0.254 (IQR = −0.025 to 0.504), whereas the median follow-up EQ-5D was 0.779 (IQR = 0.387–0.864). The difference was statistically significant (P < 0.001). The median improvement in the HRQoL was estimated at 0.508 (IQR = 0.128–0.717), which exceeds the minimum clinically important difference.[25] Despite the increase, the EQ-5D at follow-up score was still below the 25th percentile (0.894) of the general Polish population age-matched on a many-to-many basis.[13] The median preoperative HRQoL in the Visual Analog Scale (VAS) from 0 (worst imaginable health state) to 100 (best imaginable health state) was declared to be 40 (IQR = 20–50), while postoperatively, it was 70 (IQR = 52.5–80) with a median increase of 30 (IQR = 10–45). The improvement was statistically significant (P < 0.001). The median VAS EQ-5D of the age-matched general population is 80, whereas the 25th percentile is 73. A tabular display of comparison with the comorbidity-matched and age-matched datasets is presented in Table 2. Comorbidity-matched values are retrieved from the studies of Schwab *et al.*, Koga *et al.*, Hurst *et al.*, and Bond *et al.*[10,26-28]

Preoperatively, domains of health that were negatively affected most often were pain/discomfort and anxiety/depression – 94.4% of subjects reported at least moderate problems with each [Figure 1]. At follow-up, on the other hand, pain/discomfort and usual activities were disturbed the most. Preoperatively, HRQoL dimension that

Table 2: EuroQol-5 dimensions summary indices and Visual Analog Scale in craniocervical instability prior to craniocervical fixation, postoperatively, in comorbidity-matched and age-matched datasets

	EQ-5D summary index	EQ-5D VAS
Subjects with CCI preoperatively (this study)		
Entire cohort	0.254	40
Rheumatoid subgroup	0.103	20
Traumatic subgroup	0.125	35
Congenital disorder subgroup	0.187	40
Craniocervical tumor subgroup	0.535	45
Comorbidity-matched population without CCI		
Rheumatoid arthritis functional level 3	0.120	44
Spinal C1-C4 trauma	0.317	50
Congenital disorders	N/A	70
Cervical spine tumor	0.780	65
Subjects with CCI postoperatively (this study)		
Entire cohort	0.779	70
Rheumatoid subgroup	0.743	50
Traumatic subgroup	0.730	65
Congenital disorder subgroup	0.794	70
Craniocervical tumor subgroup	0.894	80
Age-matched general population	0.894*	73*

*Values representing the 25th percentile of the age-matched population. Values are presented as medians unless stated otherwise. Age-matched values are retrieved from the study of Golicki and Niewada.[13] EQ-5D: EuroQol-5 dimensions, CCI: Craniocervical instability, CCJ: Craniocervical junction, VAS: Visual Analog Scale, N/A: Not available

was the least influenced was self-care as 19.4% declared no problems at all, half of the responders had moderate difficulties, and 30.6% were unable to wash or dress themselves. At follow-up, however, walking was the area that most subjects had no problems coping with.

The medians of preoperative HRQoL in the groups with or without occiput plating were as follows: 0.100 and 0.310, respectively (nonsignificant difference; P = 0.069). The medians of the follow-up HRQoL in the same groups were 0.670 and 0.810, respectively (P = 0.061). The median increments of HRQoL in these groups were 0.540 and 0.400, respectively (P = 0.692) indicating similar results in terms of HRQoL gain in both groups. In multiple linear regression model, the outcome of interest (HRQoL at follow-up) was significantly affected by age (β = −0.004; P = 0.049) and length of the hospital stay (β = −0.134; P = 0.010). It was not influenced either by plating the occiput (P = 0.495) or neurological status upon discharge (P = 0.234) [Table 3]. A trajectory of HRQoL based on this regression model involving the significant predictors is presented in Figure 2.

Radiologic measurements

The summary of radiologic evaluation is presented in Table 4. 19.05% had at least one high-riding vertebral artery and
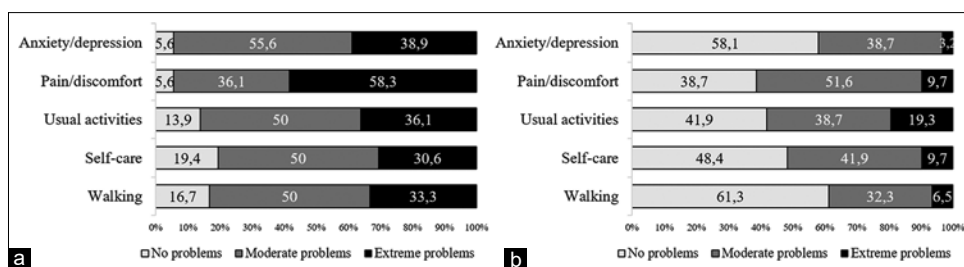
Figure 1: Distribution of the (a) preoperative and (b) follow-up domains regarding health-related quality of life in EuroQol-5 dimensions questionnaires
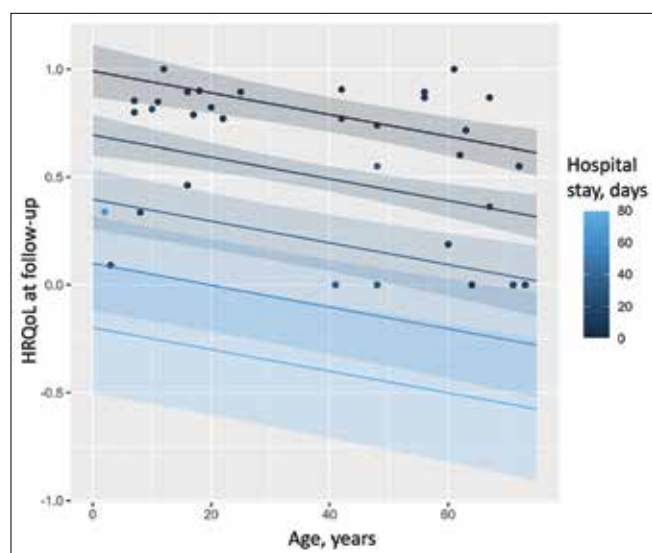

Figure 2: A graph illustrating multiple regression model with two statistically significant predictor variables (age and length of hospital stay). Health-related quality of life regarded as EuroQol-5 dimensions-3L summary index

Table 3: Summary of the multiple regression model to predict an outcome variable (health-related quality of life regarded as EQ-5D at follow-up) on the basis of four predictor variables

Variable	EQ-5D score at follow-up	
	β	P
Age (years)	−0.004	**0.049**
Occiput plating	0.073	0.495
Hospital stay (days)	−0.134	**0.010**
Neurological status at discharge	0.072	0.234

Statistically significant predictors are bolded

33.33% presented with at least 1 narrow pedicle. Parameters that were abnormal most commonly on the preoperative assessment were dens to the McRae line (71.43%) and to the Wackenheim line (60%). On postoperative scans, these two prevailed as well. Of all the classic radiologic markers, only preoperative dens to Wackenheim line correlated with HRQoL at follow-up (rho = −0.432; P = 0.028; moderate correlation). Despite the significant correlation, linear regression did not prove the preoperative Wackenheim line to be a predictor (β = −0.291; P = 0.0806). For Wackenheim parameter, Cohen's kappa of inter-software reliability was κ_1 = 0.8148, Z = 4.91 (excellent), whereas kappa of inter-observer agreement was κ_2 = 0.75, Z = 4.58 (good).

DISCUSSION

Quality of life in spinal disorders
EQ-5D scores have been established for a variety of spinal conditions. For instance, Smith et al.[29] in 2017 presented HRQoL in adult cervical deformity (ACD), of which EQ-5D-3L summary index was 0.511 (SD = 0.224). It was below the lower 25th percentile for the age-and gender-adjusted general population. Similar to our findings, the dimension of the worst quality was pain/discomfort. Better HRQoL in ACD than in CCI might be explained by the typically chronic nature of the first one. Since ACD progresses more slowly, patients are able to adapt to it, which is to the contrary of acute disorders. Therefore, subjects with acute vertebral fragility fractures demonstrate low EQ-5D-3L scores: 0.27 (95% confidence interval [CI] 0.22–0.31),[27] which is very close to the findings of the present study: 0.254 (IQR = −0.025 to 0.504). Another similarity between vertebral fractures and CCI is a substantial improvement after successful treatment. The former increases up to 0.69 (95% CI 0.66–0.72) and the latter up to 0.779 (IQR = 0.387–0.864) at follow-up.[30] It could be elucidated by the quick resolution of debilitating dysfunctions once the segments are stabilized, the pain subsides, rehabilitation begins, and fear diminishes. Moreover, as presented in Table 2, conditions that might lead to CCI (rheumatoid arthritis, cervical trauma, congenital disorders, and cervical spinal tumors) decrease HRQoL per se. Therefore, bimodal matching was executed: for comorbidities to analyze the real burden of CCI and separately for age to detect the gap between subjects after successful treatment and general population. Occurrence of CCI further exacerbates the damage and reduces life quality. As demonstrated in this study, posterior fixation of the craniocervical junction involving C1-C2 aids in this aspect, especially in terms of pain/discomfort and anxiety/depression.

Predictors of the health-related quality of life
Multiple linear regression model of four factors (chosen based on a recent meta-analysis[3]) yielded significant predictors for HRQoL at follow-up, which are age and length of the hospital stay. Older subjects and those who are hospitalized

Table 4: Summary of the pre- and postoperative radiologic evaluation

Parameter	Normal limits (mm)	Number of subjects with abnormal preoperative (%)	Number of subjects with abnormal postoperative (%)	Spearman's rho for postoperative HRQoL*	P value for rho*
ADI	<3 (a)	7/34 (20.59)	5/32 (15.63)	0.061-0.017	0.767
	<5 (p)				0.937
rCCI					
Left	<2.5	7/35 (20)	8/35 (22.86)	-	-
Right		5/35 (14.29)	8/35 (22.86)		
Dens to McRae line	≥5 below	25/35 (71.43)	26/33 (78.79)	-0.192-0.147	0.348
					0.503
Dens to Chamberlain line	<3 above	13/35 (37.14)	7/27 (25.93)	-0.139-0.347	0.509
					0.146
Dens to McGregor line	<4.5 above	13/35 (37.14)	7/27 (25.93)	-0.183-0.131	0.382
					0.593
Dens to Wackenheim line	Ventral or tangential	21/35 (60)	19/33 (57.58)	**-0.432**	**0.028**
				0.093	0.672
BDI	<8.5	7/35 (20)	7/33 (21.21)	-0.090	0.660
				0.094	0.668
BAI	−4-+12	19/35 (54.29)	13/33 (39.39)	-0.140	0.492
				0.004	0.986
Sagittal diameter at C1	>22	11/31 (35.48)	4/24 (16.67)	0.295	0.172
				0.049	0.858
Sagittal diameter at FM	>30	6/35 (17.14)	4/35 (11.43)	-0.021	0.917
				-0.069	0.747
Powers ratio		5/30 (16.67)	2/23 (8.70)	-0.416	0.054
				-0.418	0.121
Cortical breach	No breach	-	14/35 (40)	-0.090	0.677

*Upper number describes rho or *P* value of the preoperative radiologic parameter, lower number describes rho or *P* value of the postoperative radiologic parameter. Statistically significant rho/*P* values are bolded. a: Adults, p: Pediatrics, ADI: Atlantodental interval, rCCI: Revised condyle-C1 interval, BDI: Basion-dens interval, BAI: Basion-axial interval, FM: Foramen magnum, HRQoL: Health-related quality of life

for long periods might have worse health-related quality of life at follow-up. Older age is associated with lower recovery capabilities, hindered rehabilitation, and a plethora of comorbidities, all of which add up resulting in prolonged difficulties with walking, self-care, and usual activities. Although pain can often be controlled pharmacologically, disturbed activities of basic living provoke anxiety, and fear.[31] Thus, people after CCJ fusion might require further psychological help. The other factor that could predict HRQoL is duration of the hospital stay. It is often a reflection of the complications such as acute postoperative respiratory failure requiring intensive care, wound infection, or dehiscence. Interestingly, occipital plating did not prove significant here for the follow-up life quality as it did for neurological outcome in the recent meta-analysis of posttraumatic cohort conducted by Klepinowski *et al*.[3] This might be stemming from a number of different causes such as more heterogeneous cohort in the present study, lower number of subjects, or lack of direct translation from neurological status into HRQoL.

The significant Spearman's correlation rho between the Wackenheim line parameter and HRQoL should be interpreted cautiously. As Kwong *et al*.[32] demonstrated, the Wackenheim clivus line is dependent upon the neck position and, thus, at times might be unreliable. Since linear regression denied it as a predictor, the causality remains uncertain. For it was close to the threshold of significance, studies of larger samples could potentially detect it as an important early preoperative predictor of the follow-up quality of life. Moreover, as presented in Table 3, the Wackenheim parameter changed very little after the procedure. This is a sequela to the fact that the invaginated dens are often difficult to reduce, especially in rheumatoid arthritis or congenital abnormalities. In light of this information, in such situations, one should carefully consider the risk and benefits of extending surgery to transoral approach so as to decompress the brainstem.

Implications

This is the first study to touch upon the HRQoL after craniocervical instrumentation in both adults and pediatrics. HRQoL could possibly be the most important piece of outcome from the patient's perspective. There is no radiologic, laboratory, or a single clinical measure that would provide as much valuable data as life quality, yet it is often neglected in the final assessment. Knowledge of the preoperative baseline and the follow-up records could serve as background for future comparisons and discussions. Quantification of the HRQoL allows health-care providers to perform cost–utility analysis of the procedure. Appreciation of the domains of HRQoL that deviate the most after fusion

could indicate which aspects need more focus and resource allocation. Determination of the potential clinical and radiologic predictors might aid patient and family counseling, especially for the elderly and of the long hospital stay. Finally, the limitations acknowledged in this study might guide the upcoming studies to furnish stronger evidence and clinical guidelines regarding craniocervical fusion.

Limitations
Despite being contributory to the body of neurosurgical literature, this study has several flaws. First of all, this research constitutes only level 3 evidence. Although it is the best we currently have, undoubtedly studies of prospective case–control design would be appreciated to provide stronger data. Second, a number of patients could not be reached for the follow-up EQ-5D questionnaire due to an unresponsive or invalid phone number (dropout rate: 36.6%) – this was, however, taken into consideration at the stage of sample size estimation. Still, some of those unresponsive patients might have been dead or otherwise incapacitated, introducing a selection bias. This issue can only be addressed via prospective studies where it is taken into account so in such cases relatives can be reached.

Since CCI is a rare entity, the study group was heterogeneous in causes of CCJ instability. The comorbid conditions likely impact HRQoL. The authors are aware of this fact and, thus, performed matching for the comorbidities and, separately, for age. Matching for age with general population as was done here has potential to determine the gap between treated CCI and the age-matched general population. Matching for comorbidities allowed for appreciation how CCI affects HRQoL as compared with similar conditions without CCI. Overall, this is common to analyze the causes altogether due to the rarity of this condition.[7,33] Thus, large samples of each cause are possibly obtainable only through multi-institutional collaborations.

Another drawback might be that adults and pediatrics were analyzed in the same study. Even though we first considered it a limitation, it may also be considered a strong point of this work since it allowed for detection of age as an independent predictor of HRQoL at follow-up in multiple linear regression model. Moreover, in order to further mitigate the potential bias, separate subgroup analysis and HRQoL calculation were conducted for adults and children.

Posterior fixation of C1-C2 segment was performed in each subject. Some of them, however, had additional cranial or caudal extension of the stabilization. The limitation of heterogeneity of either involving the occiput or not was addressed in the subgroup analysis as well as in the multiple

linear regression model to determine whether it affected HRQoL.

As Atul Goel elegantly noticed,[34] cervical range of motion is determined mostly at the craniocervical junction (O-C2), thus inclusion of the lower cervical spine in stabilization was not addressed separately.

CONCLUSIONS

HRQoL is substantially reduced in subjects with CCI, also when compared with the comorbidity-matched dataset. Yet, it can be improved with successful posterior fixation. Despite the improvement, the HRQoL is still worse than the bottom 25th percentile of the age-matched general population. Occipital plating might not affect the trajectory of HRQoL. Patients' age and length of the hospital stay could predict HRQoL at follow-up. Elderly subjects might not benefit as much as the young from the posterior fixation in terms of quality of life. The longer hospitalization, the worse HRQoL is expected. Most of the classic radiologic markers do not correlate with one's follow-up HRQoL. Only the baseline Wackenheim line might carry such correlation, but this requires further confirmation. Results of this study could enhance patient counseling and in future might be of interest for public health when comparing posterior screw fixation with other treatment options.

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Conflicts of interest
There are no conflicts of interest.

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