Original Article

Ehlers–Danlos syndrome-associated craniocervical instability with cervicomedullary syndrome: Comparing outcome of craniocervical fusion with occipital bone versus occipital condyle fixation

ABSTRACT

Introduction: Ehlers–Danlos syndrome (EDS) predisposes to craniocervical instability (CCI) with resulting cranial settling and cervicomedullary syndrome due to ligamentous laxity. This study investigates possible differences in radiographic outcomes and operative complication rate between two surgical techniques in patients with EDS and CCI undergoing craniocervical fusion (CCF): occipital bone (OB) versus occipital condyle (OC) fixation.

Methods: A retrospective search of the institutional operative database between January 07, 2017, and December 31, 2019, was conducted to identify EDS patients who underwent CCF with either OB (Group OB) or OC (Group OC) fixation. For each patient, pre- and post-operative radiographic measurements and operative complications were extracted and compared between groups (OB vs. OC): pB-C2, clivoaxial angle (CXA), tonsillar descent, C2C7 sagittal Cobb angle, C2 long axis, and operative complications.

Results: Of a total of 26 patients, 13 underwent OV and 13 underwent OC fixation. Eighty-five percent of the patients underwent OC underwent fusion from occiput to C2, while the remaining 15% fusion from occiput to C3. Radiographic outcome in the OC versus OB group was preoperative measurements were similar between OC and OB group: pB-C2 8.8 mm (1.5, 6–11) versus 8.3 mm (1.7, 4–9.6), $P = 0.43$; CXA 128.2 (5.4, 122–136) versus 131.9 (6.8,122–141), $P = 0.41$; tonsillar descent 6.2 mm (4.8, 0–15) versus 2.9 mm (3.4, 0–8), $P = 0.05$; C2 long axis 75.2 (6.7, 58–85) versus 67.2 (21.4, 1–80), $P = 0.21$; postoperative change of CXA + 14.4 (8.8, 0–30) versus 16.2 (12.4, 4–38), $P = 0.43$; change of pB-C2 2.6 mm (1.8, -5.3 to 0) versus 1.2 mm (4, 4.6–8), $P = 0.26$; and postoperative C2C7 sagittal Cobb angle 2.6 (19.5, 43–39) versus 2.6 (11.4, 21–12). Operative complications were seen in 1 out of 13 patients (8%) versus 2 out of 13 patients (16%), $P = 1$.

Conclusions: In EDS, patients with CCI undergoing CCF radiographic and clinical outcome were similar between those with OC versus OB fixation. Both techniques resulted in sufficient correction of pB-C2 and CXA measurements with a low complication rate.

Keywords: Cervicomedullary syndrome, craniocervical instability, Ehlers–Danlos syndrome

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INTRODUCTION

In patients with hypermobile variant of Ehlers–Danlos syndrome (EDS), craniocervical instability (CCI) might be develop as a consequence of ligamentous laxity.[1-3] Resulting cranial settling with clivoaxial kyphosis leads to the clinical syndrome of cervicomedullary syndrome (CMS).[4,5] These patients frequently have concomitant descent of the cerebellar tonsil, which has been described as false Chiari Type I malformation.[4,6]

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If symptoms related to CMS and tonsillar descent are severe and refractory to conservative management, surgical treatment consisting of suboccipital decompression, clivoaxial reduction, and craniocervical fusion (CCF) may be indicated.[7,8] The primary surgical goal in this case is to reduce kyphosis between the clivus and axis (clivoaxial angle [CXA]) and to perform internal fixation between the occiput and upper cervical spine, most frequently at C2 or C3.[8,9] Correction of the CXA has been shown to correlate with postoperative clinical improvement of symptoms related to CMS.[8] Technical aspects of CCF are somewhat more challenging in these patients since they often require suboccipital decompression (SOD), which eliminates the use of a traditional occipital plate as a fixation anchor.[10] Two commonly used fixation techniques in this scenario are occipital condyle (OC) screw fixation or occipital anchors.

This study aims to investigate possible differences in radiographic outcome and operative complication rate between patients with occipital plate versus OC as the cranial fixation point for CCF in patients with EDS and CMS.

METHODS

Approval of the local institutional review board was obtained (IRB 20-0267) for the present investigation. A retrospective search of the institutional operative database was conducted to identify patients who underwent CCF with either occipital bone (OB) (Group OB) or OC (Group OC) fixation between January 07, 2017, and December 31, 2019.

Treatment of patients with suspected CMS was based on an interdisciplinary evaluation of a patient including neurologist, rheumatologist, and neurosurgeon. Diagnostic workup of a patient with clinically suspected CMS included conventional magnetic resonance imaging (MRI) of the cervical spine and posterior fossa and MRI or computed tomography (CT) of the cervical spine in flexion and extension. In patients without a formal diagnosis of hypermobile EDS, a referral to a specialist for connective tissue disorders was made. Based on clinical and radiographic impression, an MRI of the thoracic and lumbosacral spine was added (e.g., to evaluate the extend of a syrinx or to rule out tethered cord syndrome). Once the diagnosis of CCI with CMS has been established, patients have engaged in a 4–6-week trial of hard collar immobilization of the cervical spine. Improvement of the patient's symptoms during that period was observed in patients with CCI. At the end of this diagnostic workup, patients were offered surgical intervention if their symptoms were perceived as unbearable, imaging characteristics confirmed CCI, and the trial of immobilization lead to symptom relief. The surgical intervention consisted of closed reduction of the clivoaxial kyphosis, internal fixation of C0–C2 or C3 with either OC screws or occipital anchors, C1 lateral mass screws, C2 pedicle or lamina screws, and C3 lateral mass screws and suboccipital decompression (SOD) in cases of tonsillar descent. Intradural exploration to restore normal CSF flow patterns through the foramen magnum has been performed as deemed necessary. Conventionally, the choice of fixation between OB and OC has been made by the operating surgeon based on personal preference.

Patients underwent surgery under general anesthesia and neuromonitoring in a prone position with the head in the Mayfield clamp. Intraoperative neuronavigation was used for most cases, especially for the placement of OC screws. Initial exposure of the occiput and spine was achieved, using a standard midline approach from the inion down to the appropriate cervical spine level with the head in neutral position and careful dissection of soft-tissue superficial and deep layers. Following standard subperiostal exposure of the occiput, C1 posterior arch, C2 and C3 were subsequently exposed if necessary.

A 3 cm × 3 cm craniotomy window was marked in the midline above the foramen magnum. Usually, one burr hole was made 1.5 cm off midline with a pneumatic drill, followed by the craniotomy using a B2 with a footplate. The bone flap was removed. Caution was taken to identify underlying dural sinuses during exposure. In most cases, the dura was opened, and care taken not to violate the arachnoid overlying the foramen magnum. In selected cases, the arachnoid was opened, and the fourth ventricular outflow tract inspected and widened by shrinking of the cerebellar tonsils. After suboccipital decompression was achieved, occipitocervical fusion was performed using either an OB anchor (Kaspian System, K2M Leesburg, VA/USA) or OC screw (Medtronic, Dublin/Ireland).[11,12] Lateral mass, pedicle/pars interarticularis, and laminar screws were placed at C1 and C2. After confirmation of an adequate pb-C2 and CXA measurements using intraoperative computed tomography,[13-16] the rods were locked to the screws and morcellated local autograft and allograft were put in place. Figures 1 and 2 show patients with CCF using either OB anchors or OC screws.

For each patient, the following preoperative radiographic measurements were obtained: pb-C2, CXA, tonsillar descent, C2 long axis, and C2C7 sagittal cobb. The same measurements were obtained postoperative in addition to possible operative complications. A comparison of the abovementioned measurements between the two surgical groups (OB versus OC) was performed using Fisher's exact test.

RESULTS

A total of 26 patients were identified, 13 who underwent OC and 13 who underwent OB fixation as seen in Table 1. The average patient age was 31.9 years (8.6, 19.8–47.7) and 33.9 years (11.6, 21.7–58.6), respectively. Twelve out of 13 patients (96%) were female; C0–C2 fusion was performed in all cases in the OC group and in 12 out of 13 patients (92%) in the OB group.

Comparing the OC with the OB group, the average preoperative pB-C2 distance was 8.8 mm (1.5, 6–11) versus 8.3 mm (1.7, 4–9.6), $P = 0.43$, and average postoperative distance was 5.7 mm (1.3, 3.5-8) versus 5.4 (1.2, 4–8), $P = 0.54$. Average preoperative CXA was 128.2° (5.4, 122–136) versus 131.9° (6.8, 122–141), while postoperative values were 142.6° (10.8, 122–163) versus 148.1 (15.3, 118–179) [Table 2]. In both groups, tonsillar ectopia was present, which was 6.2 mm (4.8, 0–15) and 2.9 mm (3.4, 0–8), respectively. This difference between the OC and OB groups was statistically significant ($P = 0.05$). Average C2 long axis orientation in the sagittal plane was 75.2° (6.7, 58–85) and 67.2° (21.4, 1–80), respectively, with not statistically significant difference between the groups ($P = 0.21$). Sagittal profile of the subaxial spine was as follows: average preoperative C2C7 sagittal Cobb angle −2.8° (15.4, −28–16) versus − 3.1° (11.5, −21–12), respectively; average postoperative values were −2.6 (19.5, −43–39) versus −2.6 (11.4, −21–12). Operative complications were observed in one case (asymptomatic vertebral artery occlusion) of 13 for OC and two cases (pseudomeningocele and transient left arm weakness) of 13 in the OB group, $P = 1.0$.

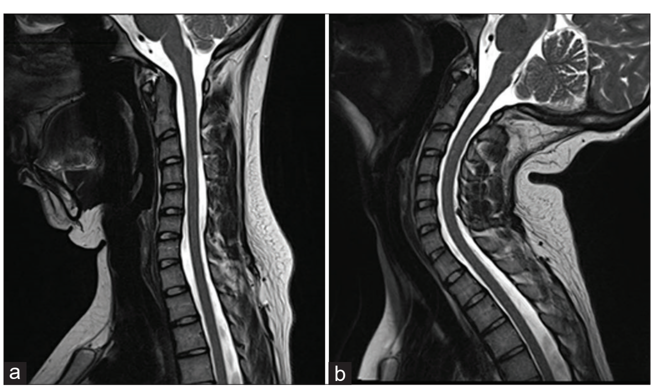

Figure 1: Sagittal magnetic resonance imaging T2 sequence in (a) flexion (left) and (b) extension (right). The following measurements relevant to craniocervical instability were obtained: flexion/extension clivoaxial angle 129°/145°, pB-C2 9 mm/5 mm, horizontal Harris measurement 12 mm/8 mm

DISCUSSION

EDS is a group of connective tissue disorders with an estimated incidence of 1 in 5000 individuals.[17] In 2007, Milhorat *et al*. demonstrated that patients with connective tissue disorders may develop CCI, which causes pivoting of the clivus on the dens and decrease of the CXA with kinking of the brain stem.[1,4] CCI may go on to manifest clinically as CMS[1] caused by ventral compression of the brain stem and cervical spinal cord.[18] Odontoid retroflection and cranial settling may further contribute to a decrease in CXA and pressure on neural elements, resulting in symptomatic presentation of CMS.[19]

In a study of 22 patients, Henderson *et al*.[4] show that the most frequent manifestations of CMS include headache, dizziness, imbalance, memory disturbance, walking impairment, vertigo, and speech disturbances.[7] Dysautonomia may also present in the form of dysuria, tachycardia, and syncope.[4,7,8] Generally, CXA <125°–135° is believed to be pathologic and a threshold for abnormality that may require surgical intervention for reduction and stabilization.[20,21] Other measures have been proposed by Grabb-Oakes who determine a pB-C2 values >9 mm pathologic for CCI.[22,23] Horizontal Harris measurement in flexion of more than 12 mm and a change between flexion and extension of more than 2 mm is pathologic.[24] Cranial settling can also cause

Table 1: Patient demographics and details of surgery

	Occipital condyle screw	Occipital bone fixation
Number of patients	13	13
Fusion levels	Condyle - C2 100%	Occiput - C3 15%, occiput - C2 85%
Age (mean, SD, range)	31.9, 8.6, 19.8- 47.7	33.9, 11.6, 21.7- 58.6
Sex (female)	100%	92%

SD - Standard deviation

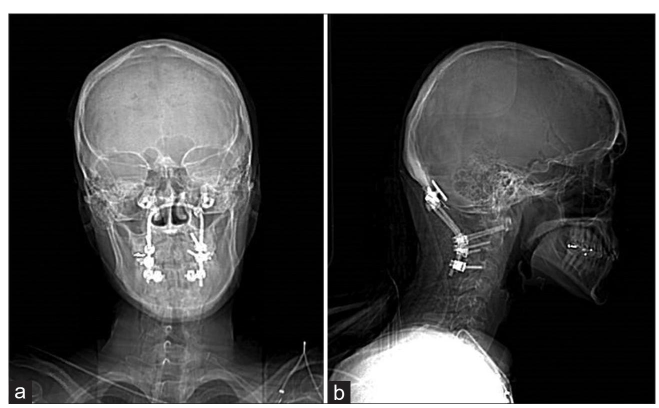

Figure 2: Anterior posterior (left) and lateral (right) X-rays of 39-year-old female patient following occipital bone to C3 fusion. Suboccipital decompression has been performed at an outside institution. (a) ap view, (b) lateral view

Table 2: Radiographic measurements before and after surgery

	Occipital condyle	Occipital bone	*P*
Preoperative pB-C2 (mm)	8.8 (1.5, 6- 11)	8.3 (1.7, 4- 9.6)	0.43
Postoperative pB-C2 (mm)	5.7 (1.3, 3.5- 8)	5.4 (1.2, 4- 8)	0.54
ΔpB-C2 (mm)	−2.6 (1.8, −5.3- 0)	−1.2 (4, −4.6- 8)	0.26
Preoperative CXA (°)	128.2 (5.4, 122- 136)	131.9 (6.8, 122- 141)	0.41
Postoperative CXA (°)	142.6 (10.8, 122- 163)	148.1 (15.3, 118- 179)	0.3
ΔCXA (°)	14.4 (8.8, 0- 30)	16.2 (12.4, −4- 38)	0.43
Tonsillar descent (mm)	6.2 (4.8, 0- 15)	2.9 (3.4, 0- 8)	0.05
C2 long axis (°)	75.2 (6.7, 58- 85)	67.2 (21.4, 1- 80)	0.21
Preoperative C2C7 sagittal cobb (°)	−2.8 (15.4, −28- 16)	−3.1 (11.5, −21- 12)	0.95
Postoperative C2C7 sagittal cobb (°)	−2.6 (19.5, −43- 39)	−2.6 (11.4, −21- 12)	1.00
Operative complications	1/13	2/13	1.00

CXA - Clivoaxial angle

tonsillar decent with similar symptoms of a classic Chiari I malformation.[25] In this case of a secondary or false Chiari I malformation, there is no posterior fossa hypoplasia, which is the hallmark of the true Chiari I malformation, [Figure 3].[25]

When CCF in patients with EDS is performed, a suboccipital decompression is often also necessary to improve CSF flow through the foramen magnum, which is impaired by the tonsillar descent. In our cohort, the mean descent of the tonsils was 6 mm and 2 mm. We determine the safe and effective result of CCF accomplished by either OC screws or occipital anchors as cranial fixation point. Previous studies demonstrate similar fixation strength between occipital plate and OC screw.[26] We anticipate a similar long-term maintenance of stability and fusion between these cohorts. Different factors related to the patient's anatomy influence the feasibility of OC screw placement such as: (1) placement of OC screw in cases of an anatomically small condyle might be difficult and (2) narrow sagittal corridor between superior aspect of the posterior arch of C1 and the hypoglossal canal might also render the placement of condyle screw more challenging.[27] The first case reportedly performed in a pediatric patient was reported in 2010 undergoing occiput to C2 fusion through OCs, C1 lateral masses, and C2 lamina achieved stable construct and fusion without neurodeficit.[28] In addition, OC screws were used in a case series involving five children for fixation of the craniovertebral junction and were found to have no complications postoperatively with CT demonstration of successful fusion.[29] In our study of adult patients, no case of hypoglossal nerve palsy or other neurological deficit has been observed postoperatively, similar to previous studies.[30,31] In a case series of 32 patients, Sasso *et al*. used posterior AO plates and transarticular screws, using the Magerl C1–2 screw technique in half of the cases with no neurological deficits postoperatively.[30] However, hardware failure related to pseudarthrosis has been reported in up to 29% without the use of structural autograft.[32]

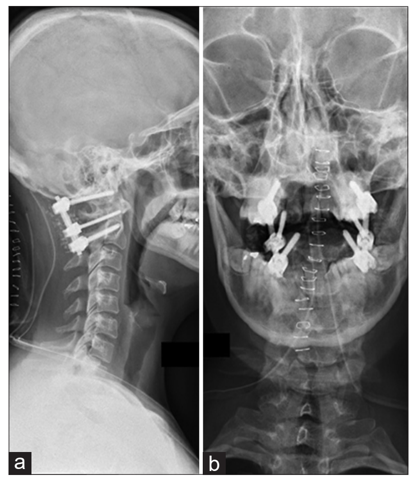

Figure 3: Anterior posterior (right) and lateral (left) X-rays of 28-year-old female patient following occipital condyle to C3 fusion. (a) ap view, (b) lateral view

In a previous study, the average CXA was corrected from 127° to 148°.[4] In another study of five pediatric patients, CXA increased on average from 126° to 147°.[7] Further, clinical improvement in this cohort was remarkable. Similar results were achieved in our study as CXA increased from 128° to 142° (+14) in the OC group and from 132° to 148° (+16) in the OB group. However, there was no statistically significant difference between the changes in angle between groups receiving this procedure. Furthermore, the average pB-C2 distance could be reduced in both groups at a similar degree, without significant differences: −2.6 mm and −1.2 mm, respectively. It is interesting to note that no significant change in the sagittal profile of the subaxial cervical spine was observed in this study.

Future studies may include a longer follow-up period to determine the long-term stability of constructs and their effects on lower level segments, degenerative disc disease, and quality of life measures. Further, an increase in sample size would support higher power in observing differences in postoperative changes in CXA between condyle screws and occipital plate methods to compare these approaches in achieving stability, restoring CXA, and sustaining long-term patient-reported outcomes and quality of life metrics. As this was a single-center study, future investigations may also incorporate these approaches in other populations with EDS to apply methods in different institutions, settings, and under the care of other surgeons. In addition, OC and OP methods may be assessed for CCI and CMS resulting from other pathologies to determine the extent to which these approaches may be uniquely tailored to treat those with EDS or other inflammatory, congenital, or traumatic causes of CCI such as rheumatoid arthritis or Down Syndrome.

CONCLUSIONS

Radiographic and clinical outcomes were similar between patients with EDS and CMS who underwent CCF with either OC screw fixation or OB plate anchors. Both approaches were safe and resulted and similar radiographic outcome.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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