

British Journal of Neurosurgery



ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/ibjn20

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To cite this article: Kazim Yigitkanli, Serkan Simsek & Aslan Guzel (2021): Posterior realignment of basilar invagination with facet joint distraction technique*, British Journal of Neurosurgery, DOI: 10.1080/02688697.2021.1914818

To link to this article: https://doi.org/10.1080/02688697.2021.1914818



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ORIGINAL ARTICLE



Posterior realignment of basilar invagination with facet joint distraction technique*

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ABSTRACT

Purpose: We describe our experience with management of basilar invagination (BI) with the atlantoaxial dislocation (C1/C2) joint reduction technique, including posterior atlantoaxial internal fixation.

Materials and methods: From 2008 to 2018, eleven patients with atlantoaxial dislocation (AAD) and BI underwent surgical reduction using C1/C2 the joint reduction technique with a fibular graft/peek cage placement followed by C1 lateral mass/C2 pedicle screw fixation. In two cases that we originally planned to perform C1/C2 joint reduction, occiput-C2 pedicle screw fixation was performed instead due to intraoperative challenges. Post-operative course and surgical complications will be discussed.

Results: A total of 13 patients, with an average age of 30.46 ± 13.23 years (range 12-57), were operated. In one patient, iatrogenic vertebral artery injury occurred without any neurological complication. JOA score improved from 10.45 ± 1.128 to 15.0 ± 1.949 (p < 0.0001, paired t-test). All radiological indices were improved (p at least < 0.001). No construct failure was seen in any of the patients with C1-2 facet joint distraction technique during follow-up, and no additional anterior decompression surgery was required. **Conclusions:** C1/C2 joint reduction technique with fibular graft/cervical PEEK cage of Bl patients together

Conclusions: C1/C2 joint reduction technique with fibular graft/cervical PEEK cage of BI patients together with AAD seems to be an effective and safe surgical method of treatment.

ARTICLE HISTORY

Received 12 September 2020 Revised 26 March 2021 Accepted 6 April 2021

KEYWORDS

Atlantoaxial; basilar invagination; distraction; vertebral artery injury

Introduction

Basilar invagination is a primary developmental anomaly that compresses the ventral brainstem and upper spinal cord.¹ In recent decades, with a better understanding of craniocervical dynamics and the advances in atlantoaxial and occipito-cervical fixation techniques, we have learned that distraction at the C1/C2 joints leads to possible reduction of basilar invagination (BI) with atlantoaxial dislocation (AAD).^{2–4}

In the present study, we summarize our experiences on BI patients with AAD who were operated by C1/C2 joint distraction reduction technique via fibula graft/cervical peek cages. Patients with BI are usually present with abnormal anatomy of the vertebral arteries (VAs) at the craniovertebral junction (CVJ) especially at the C1/2 joint level. We aim to highlight the high risk of iatrogenic vertebral artery injury and share our surgical experience to decrease the complication risk which may cause mortality and morbidity.

Patient and methods

We conducted a retrospective chart review study which included 13 consecutive patients who had BI with AAD, and underwent surgery between 2008 to 2018. Patients with AAD resulting from rheumatoid arthritis, os odontoideum, or trauma were excluded from the study. In 11 patients, the C1/C2 joint distraction techni-

ques were used, and in the other two patients, occiput-C2 pedicle screw fixation was performed.

Radiological studies

All the patients were evaluated preoperatively by plain radiographs, CT scans with reconstruction views, and magnetic resonance imaging (MRI). The ADI was measured to evaluate the horizontal dislocation of C1 over C2. The Chamberlain line (CL), McRae Line (ML), Wackenheim Line (WL) and Clivocanal Angle (CCA) were measured on sagittal CT scans. Cervicomedullary angle (CMA) was measured on sagittal MRI scans to evaluate the extent of ventral medulla and spinal cord compression by the telescopically invaginated odontoid process. The size and the anatomy of the C2 pedicle was evaluated for suitability of C2 pedicle screw fixation. The size and anatomy of C1 lateral mass, and C1/C2 facet joint, was also assessed for suitability of C1 lateral mass screw fixation and joint distraction techniques.

All patients underwent plain X-rays and CT scans with reconstructive views to define the positions of the screws and the degree of reduction early after the surgery. MRI was also performed after the surgery to assess the extent of reduction and degree of medulla and spinal cord compression.

Surgical procedure

All patients under general anesthesia were placed prone under cervical traction force using Gardner Wells (may be increased up to 1/3 of the body weights), keeping the neck in neutral position and helping reduction of the deformity (Figure 1(A)). The head of the table was elevated about 30° to decrease the blood loss. A posterior midline incision was made to expose the posterior surface of foramen magnum, C1 and C2 spinous processes. The lateral masses of the C1, C2 pars interarticularis/C2 pedicle, and C1 inferior articular process were exposed widely after bilateral sectioning of the C2 ganglion on both sides. Bilateral C1/2 joint capsules were widely removed. During removal of the joint capsule the C1/2 joint space gradually increased in height under cervical traction. The articular surfaces of the joint were decorticated by with a high-speed drill. Then, C2 pedicle screw fixations were implanted individually by directly palpating the superior-medial edge of the C2 pedicle. The facet joints were distracted by using a spreader to place the fibula graft/peek cage as a spacer (Figure 1(B,C)). In the first few cases we used 5 mm fibular grafts (Figure 1(B)) and then we started to use 5-6 mm cervical polyether-ether-ketone (PEEK) cages (LorX, Triaspine, Ankara, Turkey) that were reshaped (cut in half) intra-operatively to fit to the C1/C2 joints (Videoclip 1). 3.5-4 mm C1 lateral mass screw fixations were placed as we previously described.⁶ After doing the same procedure bilaterally, the head of the C1 and C2 screws were compressed and the heads of the screws were tightly fixed to bilateral 3.5 mm titanium rods (PS Mini, Occipitocervical System, Triaspine, Ankara, Turkey). In one patient with rotational deformity, we performed C1-2-3 internal fixation. In some patients we inserted bilateral C1/2 facet joint spacers before doing the C1/C2 internal fixation technique (Figure 1(D)).

Reduction of the deformity and the screw positions were confirmed by intraoperative fluoroscopy at the end of the procedures. The traction force was removed at the end of the surgery and the patients were placed in a soft cervical collar for ten days after the surgery.

Statistical methods

Descriptive statistics are given as total numbers, percentages, means, and medians as appropriate. BI reduction was calculated using pre and post-operative ADI, CL, WL, CMA, CCA of the 11 patients that performed a C1-2 facet joint reduction technique. JOA scoring also was recorded and compared in 13 patients that we operated. A paired Student's t-test was performed to measure BI reduction with measuring compare pre and post-operative ADI, CL, WL, CMA, CCA of the 11 patients that we performed C1-2 facet joint reduction technique. Statistical analysis was performed using GraphPad Prism (GraphPad software version 6, San Diego CA, US).

Results

A total of 13 patients (seven male and six female patients) with average age 34.46 ± 13.23 years, ranging from 12 to 57 years were operated.

Clinical features

The clinical characteristics are summarized in Table 1. Patients presented with numbness in extremities (n = 13), neck pain (n=10), quadriparesis (n=10), voice change (n=5), respiratory

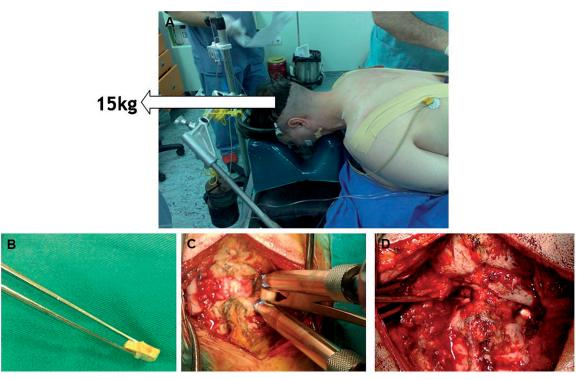


Figure 1. The patients under general anesthesia were placed in a prone position under cervical traction force using Gardner Wells (may be increased up to 1/3 of the body weights), keeping the neck in neutral position and helping for the reduction of the deformity (A). Fibula graft to insert to C1/2 facet joint as a spacer (B). Intraoperative photograph while inserting the fibula graft to the C1/2 facet joint and using C1 lateral mass and C2 pedicle screws for distracting the joint space to open space for the graft (C). Intraoperative photograph showing intraoperative reduction of the BI and AAD with bilateral facet joint distraction technique. C1/2 facet joint reduction was achieved by inserting peak cages as spacers to C1/C2 joint before C1/C2 screw fixation (D).

difficulty (n=4), torticollis (n=3), hemiparesis (n=2). The most common symptom was numbness in the extremities followed by neck pain. The neurological status of the patients were evaluated by the Japanese Orthopedic Association (JOA) scoring before and after the surgery. Occipitalization of the atlas as observed in 12 of 13 patients. Four patients had associated Chiari malformation and four patients had rotational deformity at the C1/C2 level (Table 2).

Surgical data results

The operative time ranged from 90 to 200 min and blood loss ranged from 90 to 400 ml. Among the 13 patients, C1 lateral mass and C2 pedicle screw fixation technique was performed in 11 cases. The C2 nerve roots were resected in all 11 patients bilaterally who underwent C1/C2 joint distraction technique. Bilateral C2 pedicle screw fixation was possible in all 13 patients, which were carefully evaluated preoperatively for the high riding vertebral artery anomaly at the C2 pedicle level. In two patients, Occiput-C2 pedicle screw fixation technique was performed differently from the preoperative plan due to intraoperative complications. In one case, major bleeding from the venous plexus at C1/C2 joint surface was encountered so suboccipital screws instead of C1 lateral mass screw fixation was performed. In the other case, surgical accidental VA injury at the C2 ganglion sectioning stage occured. The right VA was posterior to C1/C2 facet joint ventral to the C2 ganglion which was not realized pre and intra-operatively. During the dissection and sectioning of the right C2 ganglion the right VA injury caused arterial bleeding which was controlled by inserting hemoclips to the right VA. We did not try to dissect the left C1/2 facet joint and completed the surgery with Occiput-C2 pedicle screw fixation. In both cases we

Table 1. Clinical symptoms of 13 patients with basilar invagination.

Clinical features	Number of patients
Numbness of Limbs	13
Neck pain	10
Quadriparesis	10
Voice change	5
Respiratory difficulty	4
Torticollis	3
Hemiparesis	2

applied lever forces to these screws under cervical traction force to achieve some degree of reduction without C1-2 facet joint cage/graft application. In four patients who had Chiari malformation, an additional suboccipital bone decompression was performed without opening the dura.

Postoperative clinical parameters

Using the preoperative and post-operative JOA scoring all the patients had improvement (100%). Clinical follow ups ranged from 14 to 130 months (59.08 ± 35.67). Mean JOA scoring after surgery at the last follow up was 15.0 ± 1.949 compared to preoperative JOA scoring of 10.45 ± 1.128 (p < 0.0001, paired t-test) (Figure 2).

Radiological follow-up

Figure 3 shows the pre and postoperative radiological outcomes. The ADI decreased significantly from $8.36 \pm 3.66 \,\mathrm{mm}$ to $2.92 \pm 1.82 \,\mathrm{mm}$ postoperatively (p < 0.0001, paired t-test). The cervicomedullary angle increased significantly from 130.2°±9.3° to $147.7^{\circ} \pm 9.94^{\circ}$ postoperatively (p < 0.0001, paired t-test). CCA increased significantly from 116.7°±11.96° to 133.9°±10.32° (p < 0.0001, paired t-test). There was a significant reduction of BI as assessed by using Chamberlain Line 14.84 ± 7.44 mm to 7.34 ± 7.87 mm, (p < 0.0001, paired t-test). Wackenheim Line decreased from $10.18 \pm 6.54 \,\mathrm{mm}$ to $2.44 \pm 4.73 \,\mathrm{mm}$ (p < 0.001, paired t-test) and McRae Line decreased from $7.04 \pm 1.60 \,\mathrm{mm}$ to $2.28 \pm 1.86 \,\mathrm{mm}$ (p < 0.0001, paired t-test) (Figure 4). In four patients, because the posterior margin of the foramen magnum was removed it was not possible to draw CL and ML postoperatively so an alternative method of measurement was used which was previously described.

MRI showed good decompression of the medulla and spinal cord in all the patients (Figures 4 and 5). There was no construct failure and no motion were observed in dynamic radiographs of the patients with atlantoaxial joint reduction technique. None of the patients required additional anterior decompression surgery.

Complications

In one patient with intraoperative VA injury, there was no postoperative neurological deterioration. When we evaluated the

Table 2. Operated basilar invagination patients with associated radiological anomalies, performed surgery type, clinical outcome and follow-

Patient no.	Age				JOA score		
		Sex	Radiology	Surgery	Pre-operative	Post-operative	Follow-up (months)
1	13	М	C1A, RD	C1-2	12	15	130
2	36	M	C1A, Ch	C1-2	12	16	104
3	36	F	C1A	C1-2	11	16	101
4	38	M	C1A, Ch	C1-2	9	13	81
5	26	F	C1A, Ch	C1-2	11	16	60
6	12	F	C1A, RD	C1-2	11	13	57
7	17	F	C1A	C1-2	11	16	55
8	48	F	C1A, RD	Oc-C2	11	16	51
9	25	M	C1A	C1-2	7	11	35
10	57	F	C1NA	C1-2	10	16	34
11	22	М	C1A, Ch	Oc-C2	10	16	28
12	31	М	C1A, RD	C1-2-3	13	16	18
13	35	M	C1A	C1-2	12	15	14

M, male; F, female; C1A, C1 arch assimilated with occiput; C1NA, C1 arch not assimilated with occiput; RD, Rotational deformity; Ch, Chiari malformation, Syr, syringomyelia; Oc-C2, occiput-C2 screw fixation with joint distraction technique performed, C1-C2, C1 lateral mass and C2 pedicle screw fixation with joint distraction technique performed; pre-op, preoperative; post-op, postoperative.

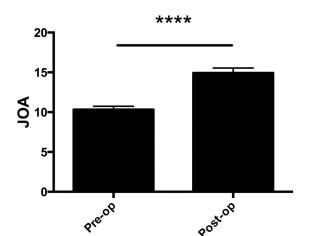


Figure 2. Bar graph representing the pre and post-operative neurological recovery comparison (JOA score) as mean (ranges) \pm SD in all 13 patients. Statistical analysis were done as paired *t*-test; ****Pre vs Post-operative statistical comparison (p < 0.0001).

preoperative cervical CT of this patient in detail we realized the bilateral anomalous course of the VAs (Figure 6). There was no mortality in our series.

Discussion

Direct posterior C1/C2 joint manipulation and reduction techniques does not have the potential complication risks of anterior surgery and gives effective and sustained reduction with a single posterior approach.

Traction and reduction

Our group previously showed that traction may pull down the odontoid process away from the brain stem in basilar invagination cases, especially in patients without Chiari malformation, resulting clinical and radiological improvement. This observation suggests that a relative vertical instability persists in the

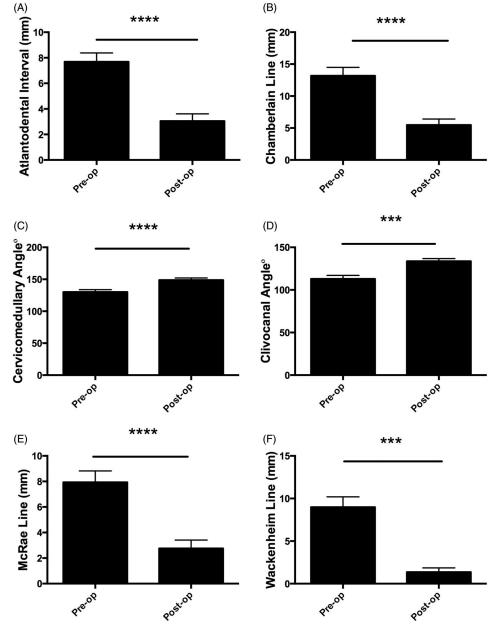


Figure 3. (A–F) Bar graphs representing the pre and post-operative radiological measurement results as mean (ranges) \pm SD in 11 patients that we performed C1-2 facet joint reduction technique. Statistical analysis were done as paired *t*-test; pre vs post-operative statistical comparison. ****p < 0.0001; ***p < 0.0001.

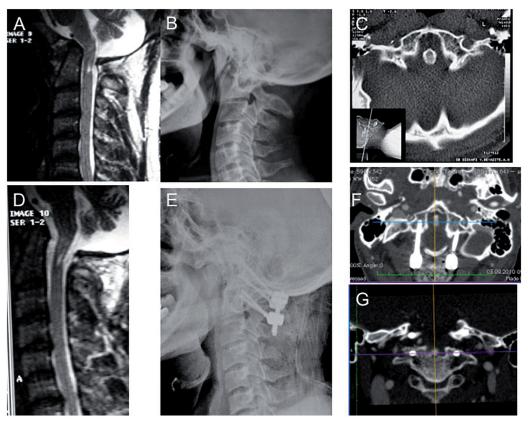


Figure 4. A 39-year-old man presented with paresthesia and weakness in all four limbs. Preoperative sagittal MRI (A), lateral radiograph (B) and axial CT scan (C) and indicated severe medulla compression with AAD and Bl. C1/C2 joint reduction technique and C1 lateral mass and C2 pedicle screw fixation technique was performed. Post-operative sagittal MRI (D) and lateral radiograph (E) showed complete reduction of the deformity with C1 lateral mass and C2 pedicle screw fixation with joint reduction technique. Post-operative axial CT scan through the C1 level (F) shows bilateral C1 lateral mass screws (F) and coronal CT scan (G) shows bilateral C1 lateral mass screws in the occipitalis atlas and bilateral C2 pedicle screw fixation technique.

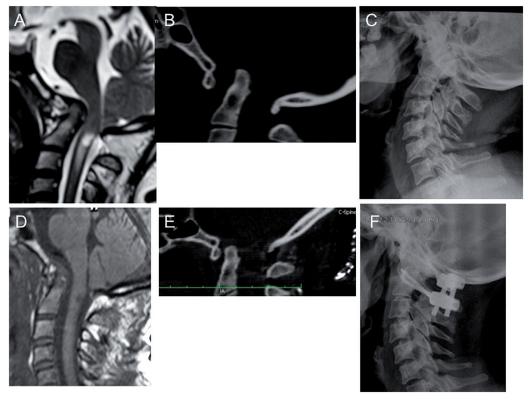


Figure 5. A 36-year-old woman presented with paresthesia and weakness in all four limbs. Preoperative sagittal MRI (A), sagittal CT (B) and lateral X-ray (C) indicated severe medulla compression with AAD and BI with occipitalization of the atlas. C1/C2 joint reduction technique and C1 lateral mass and C2 pedicle screw fixation technique nique was performed. Postoperative sagittal MRI (D) and sagittal CT scan (E) showed complete reduction of the deformity with complete reduction of ADI. Post-operative lateral X-ray (F) also demonstrated the C1 lateral mass and C2 pedicle screws.

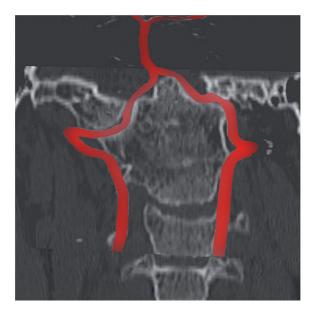


Figure 6. Reconstructive coronal CT image of the patient that iatrogenic vertebral artery injury occurred. This image was not created and seen before the surgery. VAs curve below the occipitalis atlas lateral mass at the C1-2 facet joint level then enter the cranium (This image was not originally a CT Angiography but reconstructive images of the patient was created after the surgery which VA injury occured to see the anomalous course of the VAs).

craniovertebral region. But to maintain this reduction at follow up is a major difficulty. Goel et al.² reported four patients in whom posterior fixation was performed with in situ reduction of basilar invagination and atlantoaxial dislocation; however, all the patients needed transoral decompression surgery at a later stage because the reduced position could not be maintained by the implant. We also had a similar experience; even though we had performed reduction of the basilar invagination with halo-traction, the failure of the occipital screws required the revision of the construct at the follow-up period that additional transoral decompression surgery was required (unreported data). As a result, we started to use intraoperative traction as just the initial part of our treatment protocol. In basilar invagination cases, performing atlantoaxial joint arthrodesis to further distract the C1-2 joint to avoid further cranial settling and create a new fusion area to resist powerful traction forces of this deformity may be a better way of reduction of the deformity also avoiding failure of the internal fixation device.

C1/C2 facet joint reduction

Goel was the first to hypothesize that the abnormal angulation of the C1/C2 joints were the cause of superior migration of the odontoid process, causing vertical instability of the CVJ in BI.^{2,3} As for pointing out the cause of the pathology, Goel and colleagues²⁻⁴reported C1/C2 facet joint distraction with spacers under the cervical traction force completed by C1/C2 screw and plate fixation to successfully operate these points. Chandra et al.^{8,9} also used a C1/2 facet joint distraction technique under cervical traction, completed by C1 lateral mass-C2 translaminar or in atlas assimilation cases Occiput-C2 translaminar screw fixation techniques In later studies Yin et al.¹⁰ published their experience as modified Goel's technique. After opening the C1/C2 facet joint and making it fully mobile, by intraoperative manipulation acting on this facet joint, they drew the C1 backward while pushing the

C2 downward and forward without using cervical traction force. ¹⁰ All these studies support the idea that the main target to fix the BI pathology should be in opening, fully mobilizing, and distracting the C1/C2 facet joint with specially designed distraction cages/grafts on both sides. We used fibula graft/cervical peek cages to distract these joints. Cages were reshaped intra-operatively (cut in half) and the holes inside the cages or fibula grafts were used to put allograft material inside to provide better bony fusion. Further distraction, compression, and extension reduction may also be done according to the degree of the reduction by applying lever forces to these spacers as previously described.^{8,9,11} By using this technique we achieved statistically significant and long term reduction of BI in all radiological parameters (Figure 2).

C2 ganglion sectioning

Preparation of the C1 lateral mass inferior articular process and dissection and arthrodesis of C1-2 articular surfaces may be a relatively difficult procedure in occipitalis atlas which is commonly associated with BI as in our series. Bilateral sectioning of the C2 ganglion yields better dissection and visualization of the region, resulting in better C1/C2 joint distraction technique. It also helps to control the huge venous bleeding. According to patients' subjective feeling they experience hypoesthesia at the C2 dermatome at the early post-operative period, and the area of numbness progressively reduces in size and does not cause major complaints at longer follow-up. C1 lateral mass and C2 pedicle screw fixations were also easier and safer to perform after opening the facet joint due to better orientation to this complex pathological anatomy according to our sense.

Atlantoaxial fixation (C1 lateral mass/C2 pedicle screw fixation)

Occipitocervical fixation is a widely used technique, and its clinical outcome has been reported to be satisfactory in the stabilization and performing effective reduction maneuvers to this region.² Our group previously reported occipitocervical fixation and reduction maneuvers. 12 We believe C1 lateral mass screw fixation is a better surgical option in BI cases compared to occipital screw fixation. The width of the occipital bone is reported to be commonly short in CVJ pathologies. Our method of using C1 lateral mass screws with longer screw trajectory gives better screw purchase compared to shorter suboccipital screws. Additionally the use of C1 lateral mass screws may avoid the risk of posterior fossa hemorrhage caused by suboccipital screws penetrating the occipital bone. We described our free hand C1 lateral mass screw fixation technique previously.¹³ To better evaluate the patients and possible variations of the region, preoperative detailed radiological examination helps us to prevent intraoperative complications due to C1 lateral mass fixation technique. 6,13,14 Furthermore C2 pedicle screws have more stability in lateral bending and axial rotation than C2 translaminar screws. 10 In addition, the increased biomechanical strength of the C1 lateral mass screws, and C2 pedicle screw fixation gives opportunity of further distraction and reduction of the deformities with a better way of resisting construct failure in BI. We also believe that C2 translaminar screw should only be an alternative strategy if C2 pedicle is not suitable to perform due to high riding vertebral artery or intraoperative difficulties. Sometimes atlantoaxial fixation may be a challenging surgical procedure, related to factors like massive venous bleeding, VA injury risk or anatomical

variations like fused atlas anomaly, which are commonly observed in BI as in our series.^{8,9} If C1 lateral mass or C2 pedicle screw fixation techniques were not possible, occiput-C2 pedicle or C2 translaminar screw fixation should always be kept in mind as an alternative internal fixation strategy. In two patients in our series, different from the preoperative plan, we performed Occiput-C2 pedicle screw fixation. One of them was due to huge bleeding from the venous plexus and in the later case, abnormally coursed vertebral artery was injured intra-operatively so no further risk was taken to insert C1 lateral mass screws.

Vertebral artery injury risks

Vertebral artery injury risks should always be considered again and again in posterior craniovertebral junction fixation surgeries. When C1 arch is fused with occiput there is significant increase in incidence of VA anomalies.¹⁵ Chandra PS et al.⁸ found anomalous VA in 21 of 51 (41.4%) in patients with BI and AAD with occipitalized atlas. The VA was found over the joint surface in 10 of 51 (20%) patients which increase iatrogenic VA injury risk during dissection of the C2 ganglion before C1-2 facet joint reduction.⁵ Following iatrogenic VA injury in four of their patients they started to perform CT Angiogram with 3D reconstruction before surgery in their series similar to our experience. Wang et al.⁵ classified variations in VA in the presence of an occipitalis atlas into four types on 36 patients and 72 VAs. Type I, wherein the VA enters the spinal canal below the C1 posterior arch, and the course of the VA is below the occipitalis C1 lateral mass (8.3% of 72 vertebral arteries); Type II, the VA enters the spinal canal below the C1 posterior arch, and the course of the VA is on the posterior surface of the occipitalis C1 lateral mass, or makes a curve on it (25%); Type III, wherein the VA ascends externally laterally after leaving the axis transverse foramen, enters an osseous foramen created between the atlas and occipital bone, then into the cranium (61.1%, most common variety); and Type IV, in which the VA is absent (5.6%).

C1/C2 facet joint distraction technique can be dangerous in cases of a persistent first intersegmental artery, where the VA courses abnormally below the C1 posterior arch (type I or II) of Wang's classification.⁵ Until the iatrogenic VA injury in our patient we were not routinely performing CT Angiography as a pre-radiological routine examination in our BI cases. Since then we are using CT Angiography as pre-op work up (unreported data). Routine preoperative CT angiogram should be performed and carefully examined in all patients, which were planned to undergo facet joint distraction technique. If an abnormal VA is diagnosed preoperatively this part of dissection should be performed under a microscope with vascular microsurgery set ready for anastomosis. If an abnormal VA exists it would be positioned ventral to the C2 ganglion and posterior to the C1-2 facet joint. Since we are always cutting the C2 ganglion according to our surgical technique it should be carefully dissected and separated from the abnormal VA. The dissection stage of the surgery sometimes is challenging to huge venous bleeding. Preoperatively knowledge about the dominat VA side is also significant. Starting the dissection from the non-dominant VA or normal VA course is required, with one sided C1-2 facet joint dissection at the normal VA side may also be advisable as an alternative.

Alternative surgical method of treatment, direct posterior occiput-C2 reduction or C1/C2 fixation without opening the C1/ C2 facet joint may be a strategy in BI with AAD patients who had anomalous VA course.7

We did not have VA injury due to C2 pedicle screw fixation in our series, as we performed a detailed examination of preoperative CT scans for high riding VA and palpated and targeted the superomedial border of C2 pedicle during screw fixation. In the literature, VA injury during C2 screw fixation may occur 2% to 8.2% of cases in case of high riding VA at the C2 level. 16

Conclusion

C1/2 facet joint distraction with atlantoaxial fixation under intraoperative cervical traction forces gives the better chance of reduction of the deformity, and helps to keep the reduced position of the deformity in long term follow-up of basilar invagination cases with AAD.

Authors' contributions

SS and KY performed the study and surgeries. AG contributed to the surgeries. KY contributed image and data interpretation, the writing of the article, and study design. SS contributed to data interpretation and scientific advice. AG contributed to the data All authors and approved interpretation. read final manuscript.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee (name of institute/ committee) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This is a retrospective chart review study which complies with the country's ethical requirements and law. No other specific requirements were required according to the national law of authors' country.

Consent for publication

Informed consent for the surgery was obtained from all individual participants included in this retrospective study.

Acknowledgement

The authors thank Arda Yigitkanli, Georgia Tech Biomedical Enginering Student, US for kindly editing the grammar of the manuscript.

Disclosure statement

The authors declare that they have no competing interests. All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patentlicensing arrangements), or non financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

Data availability statement

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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