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# Current insights and surgical interventions in craniovertebral junction instability. A systematic review and meta-analysis

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#### **A**BSTRACT

Background: The Craniovertebral Junction (CVJ) is prone to various pathologies, including instability and congenital anomalies. Understanding these conditions and their management strategies is critical for effective treatment.

Materials and Methods: A systematic search was conducted in Science Direct and PubMed databases following PRISMA guidelines. Inclusion criteria encompassed studies addressing craniovertebral instability and associated pathologies. Six systematic investigations were assessed for methodological quality. Data extraction involved 702 patients with CVJ issues, among which 129 had related conditions, while 279 displayed normal CVJ. Surgical interventions encompassed various techniques such as C1-C2 fixation, posterior decompression, and screw placements.

Results: Among 702 patients studied, atlantoaxial subluxation, basilar invagination, and odontoid fractures were observed in 129 cases. Surgical treatments showed favorable outcomes, with fusion achieved within a year post-surgery for both C1-C2 fixation techniques and posterior decompression strategies. Studies highlighted successful outcomes in cases of cervical myelopathy, especially with early occipitocervical fusion.

Conclusion: Managing atlantoaxial instability remains a debated topic, with varying success rates observed in different surgical interventions. Recommendations emphasize the importance of stabilization techniques and imaging modalities for effective preoperative planning and postoperative care. However, limitations in available data underscore the need for further research to refine treatment strategies for better patient outcomes in this complex area of spinal pathology.

#### Keywords

craniovertebral junction, atlantoaxial, instability, basilar invagination,



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#### INTRODUCTION

The Craniovertebral Junction (CVJ) constitutes a critical juncture susceptible to various pathological conditions encompassing infections, inflammations, degenerative disorders, neoplasms, and congenital anomalies, such as severe deformities and neurological impairments [1]. Emerging genomic associations, particularly within the fibrillin gene (FBN1). underscore its linkage malformation, Basilar Invagination, and atlantoaxial dislocation [2]. Notably, a significant correlation exists between specific gene variants in newborns Marfan syndrome and morphological irregularities observed in C1-C2 joints among patients experiencing basilar invagination and atlantoaxial dislocation [2].

Remarkably, around 84 syndromes are believed to be intricately connected to CVJ, including both autosomal dominant and recessive forms, often within chromosomal regions like 3p21.1-14.1. Among these syndromes, Larsen syndrome stands out, characterized by deletions in filamin B, a protein crucial for actin binding [3].

The atlantoaxial joint, recognized as the most mobile joint in the neck, embodies a predisposition for instability, allowing extensive circumferential movement owing to its unique articular surfaces, which can vary from rounded to flattened. While instability is common in this joint, its structural variability facilitates motion, albeit with potential complications. Anomalous atlanto-dental alignment captured during neck flexion and extension aids in identifying atlantoaxial instability, which manifests in various forms—vertical, lateral, circumferential, central, or axial—resulting in misalignment of the facet bases [4].

Furthermore, the connection between basilar invagination (BI) and irreducible atlantoaxial dislocation poses a grave concern, as the protrusion of the bulb can compress the cervical spinal cord, potentially leading to irreparable spinal cord injury or stenosis and subsequent limb dysfunction. Advanced imaging technologies like computed tomography (CT) enable precise examination of affected regions, with the primary objective being the correction of atlantoaxial instability to address basilar invagination [5].

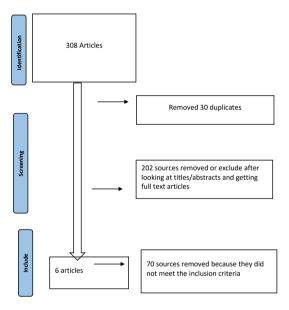
This article aims to synthesize the most current insights into craniovertebral junction instability, particularly in patients presenting with concomitant

pathologies, emphasizing the critical goal of stabilization.

#### **MATERIALS AND METHODS**

#### **Search Strategy and Selection Criteria**

A systematic search strategy was executed in the Science Direct and PubMed databases utilizing Mesh terms encompassing Craniovertebral Junction Diseases, Atlanto-Axial Joint, Fusion of C2-C3 Vertebrae, Basilar Invagination, and related pathologies. The search encompassed articles from database inception until August 2023, aligning with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Adhering to the PRISMA guidelines, the search process involved meticulous screening of articles (Figure 1).



**Figure 1**. PRISMA protocol outlining the systematic review and meta-analysis of CVJ Atlantoaxial instability.

#### Inclusion/Exclusion Criteria

The search strategy was structured around comprehensive Mesh terms and keywords linked to diseases associated with basilar invagination, C2-3 fusion, atlantoaxial instability, and craniovertebral junction instability.

Inclusion criteria comprised:

- Analysis addressing craniovertebral instability associated with pertinent pathologies.
- Investigations focusing on atlantoaxial dislocation and the progression, alterations, and stabilization of craniovertebral instability.

#### Criteria for Exclusion

- Exclusion of patients under 18 years without known medical conditions related to the craniovertebral junction or atlantoaxial instability.
- Elimination of cases that did not meet the specified inclusion criteria.

#### **Data Extraction**

Data extraction encompassed comprehensive retrieval of relevant information, including atlantoaxial instability, C2-3 Fusion, Basilar invagination, demographic details, interventions, controls, and pertinent methodologies, following standardized protocols in alignment with the study parameters.

#### Risk of Bias Assessment

The methodological quality of six systematic investigations was evaluated using the risk of bias assessment technique.

#### **Analytical Statistics**

Summary statistics such as mean difference and odds ratio (OR) were utilized for each relevant occurrence. Outcomes of interest and specific data extracted from included studies were defined using weighted mean difference (OR) and 95% confidence interval (CI). Statistical significance was set at P < 0.05 for main and subgroup analyses. Analysis software employed included Review Manager, Rayyan version 5.3, Jasp, and GraphPad 8.0.

#### **RESULTS**

The review encompasses various studies focusing on cervical spine and craniovertebral junction (CVJ) conditions and surgical interventions. In this systematic review, 308 articles were found using the various databases previously mentioned. We then went ahead and eliminated 30 duplicates and 202 articles that did not fit the criteria for our study, regardless of whether they were full texts, titles, abstracts, or any combination of these. Six publications were included for the standard base of our study after 70 articles that did not fulfill the inclusion criteria were removed, in accordance with the PRISMA systematic review process. fig. As stated by the writers, particularly Chang et al. [6]. conducted a retrospective analysis of 129 instances, with the control group accessing 297 cases for 44% of CVJ patients' C1-C2 fixation and decompression.

For instance, the authors state that previous research support their paper by measuring the various techniques. See the table for methods that bolster the study, the most common decompressions at the C1-C2 level, the various scales that have been demonstrated, development of craniovertebral approaches in the treatment of their instability, and the favorable reaction to these kinds of methods. 1. Figure 2 shows an illustration of research on craniovertebral instability, and Figure 3 shows the placement of the transperdicular screw insertions in C2 and the lateral mass of C1. Figure 4 of a research in Excel compares the many unstable craniovertebral diseases. The cerebellar amygdalae and brainstem of a 3-year-old child are observed to be shifted downward, which may be an indication of Chiari type II associated with instability of the craniovertebral junction. B.

A remarkably lengthy syringomyelia exhibiting scoliosis stretched from cervical level 6 to the lower thoracic levels. C. A young child undergoing craniocervical decompression has both Chiari type 2 and cervical syringomyelia. D. At the level of C1-C2, a severe herniation of the cerebellar amygdala and related brainstem, which is symptomless, is caused by an expansion of the spinal canal and foramen magnum. [Twenty]. as seen in figure 5. Figure 6. Error standard against effect size radial diagram Our metaanalysis indicates instability of the craniovertebral junction. The Smart Iris imaging system in Taiwan conducted a retrospective comparative study involving 702 consecutive patients who underwent MRI examinations of their cervical spine or CVI junctions. Among these, 129 had CVJ issues, 279 showed normal CVJ, and there were 294 controls (p=0.009). The normal CVJ group had significantly fewer male patients (15%) compared to the diseased CVJ (34%) and control (61%) groups. Conditions observed included atlantoaxial subluxation, basilar invagination, and odontoid fractures. [6].

One study evaluated 140 patients with posterior arches of the C1 vertebra measuring >4 mm. Treatment options involved fixing the lateral mass or screw-fixing the C1 pedicle. Both groups achieved fusion within a year post-surgery, with group A procedures taking less time and using less blood than group B (p<0.05). [13]. Another investigation focused on 81 cases of atlantoaxial instability treated with C1 and C2 screws. Despite some screw placement issues, the fixation technique was

deemed effective for patients of all ages. [19]. In a Korean study of 32 CVJ lesions, various causes were identified, including rheumatoid arthritis, traumainduced instability, tumors, and basilar invagination. Different surgical approaches were taken, such as posterior decompression with fusion, transarticular screw fixation, and anterior decompression with fusion. Most cases of cervical myelopathy showed clinical improvement, especially when early occipitocervical fusion was recommended. [21]. A study involving young Down syndrome patients (38 out of 1056) with CVJ instability reported various symptoms such as myelopathy, paralysis, gait

abnormalities, discomfort, and torticollis. Surgical interventions included internal fixation using different graft structures, resulting in reduced external orthotic needs. However, there was a 3% mortality rate and a 36% morbidity rate. [22]. Additionally, a study on occipitocervical fusion and biomechanical stabilization in cases of craniocervical instability reported successful fusion in 16 cases over an average of 35 months, with few complications and improvements in Nurick scores. [23].

State the following. Relative studies are shown in Table 1 below.

Table 1.

Author	Year	Kind of study	Cases	Control	Pathology aso. CVJ	Localization	Approaches	Means measures pre-	Post operation	Follow up	P-value
Chang et al. [6].	2021	Retrospective comparison study	129/7 02	294	Rheumatoi d arthritis	C1-C2	Screw fixation	1.6 7 ± 0.5 1 cm <sup>2</sup>	1.0 3 ± 0.3 9 cm <sup>2</sup>	1-2 Years	p=0.0 01
. Singh et al. [3].	2020	Retrospective, observational study (Pediatric population).	10	N/A	Larsen syndrome	C1–C2 instabili ty	Screw fixation /Descm	4	2	86 months /2	<i>P</i> < 0.05
Goel et al. [8].	2005	Review article 20 years of experience	160	N/A	CVJ atlantoaxial instability, Syringomyeli a Basilar invagination	C1-C2 Atypical vertebr ae	Screw fixation /Descm	3.5	2	3 months	N/A
Dastagirza da et al. [7].	2023	Review	60	206	CVJ instability Chiari Malformati on I	C1-C2	Screw fixation /Descm	0.7 2- 0.7 6	2.7	6-12 months	N/A
Joaquim et al. [12].	2023	Systematic review	23 Studies	8/123 3	Basilar invagination	C1-C2	Screw fixation /Descm	0.6	1.1 8	-	N/A
Yan et al. [13].	16	RCT	140	N/A	Atlantoaxial instability C1	C1-C2	Lateral screw fixation	1.8	1.4	13 months	<i>p</i> < 0.0
	2016										

Salunke et al. [15].	2021	Retrospectiv ely analyzed	268	17	Chiari and vertebral artery injury	C1-C2	C1-C2 fixation	7.3	0.48	6-12	(p < 0.01
Lohkamp et al. [16].	2022	Systematic review	78	N/A	Craniocervi cal Instability in Ehlers- Danlos Syndrome	C1-C2	the clivo-axial angle (CXA	5	4	6 Mont hs	N/A
Ottenhaus en et al. [17].	2023	Narrative review	212	N/A	Chondroma	C0-C2	Fixation	2	4	-	-
Ramírez- Paesano et al. [18].	2023	Review	2 studies	N/A	Ehlers- Danlos Syndrome	C1-C2	occipitocervic al fixation	4.3	2.6	N/A	N/A
Guvin et al. [19].	2018	Retrospectiv e cohort analysis	43	N/A	Traumatic- Rheumatoi d arthritis	C1-C2	C1-C2 fixation	1	0.3	N/A	N/A
Encarnaci ón-S D. et al. [20].	2023	Retrospective study	100	N/A	Chiari type II	C1-C2	CVJ descomprens ión	1.5	1.7	6-12 mont hs	(p 0.01)

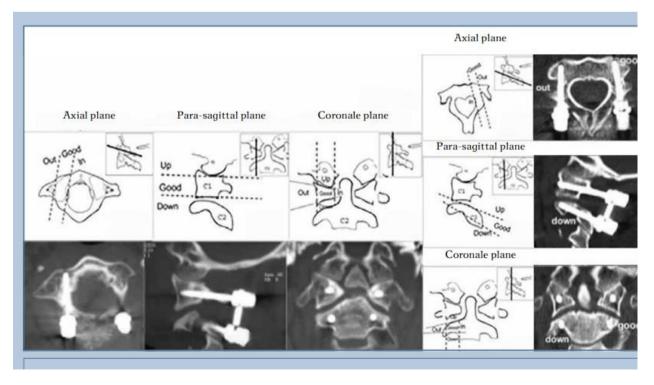
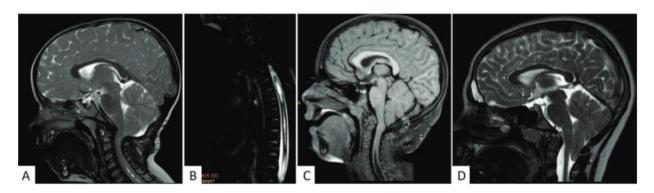
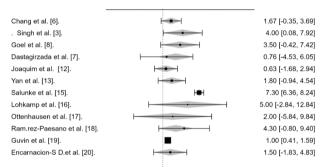


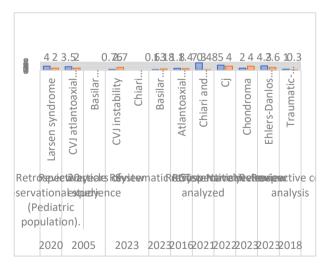
Figure 3. The location of the screw that was transpedicularly inserted into C2 and placed into the lateral masses of C1 [9].



**Figure 5.** A 3-year-old child's brainstem and cerebellar amygdalae are seen to be displaced downhill, representing a potential example of Chiari type II connected to instability of the craniovertebral junction. B. An extraordinarily long syringomyelia with scoliosis extended from C6 to the lower thoracic levels. C. Cervical syringomyelia and Chiari type 2 are present in a young patient having craniocervical decompression. D. At the level of C1-C2, an extension of the spinal canal and foramen magnum results in a severe herniation of the cerebellar amygdala and associated brainstem, which lacks symptoms. [20].



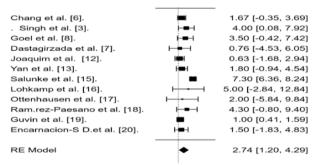
**Figure 2**. Shows the group effect size of consequence studies for craniocervical junction instability.



**Figure 4**. Craniovertebral junction studies and, approaches with pathologies associates

#### DISCUSSION

These studies emphasize the importance of understanding the surgical anatomy and structures



**Figure 6.** Standard error vs Effect size Radial plot Craniovertebral junction instability

involved in CVJ instability. They highlight the necessity of preventing damage to the vertebrae, especially C1 and C2, and the significance of the vertebral artery's course and groove in surgical planning. Atlantoaxial alignment was evaluated based on facet alignment during neutral head positioning. [9]. Different types of atlantoaxial facet instabilities were identified, emphasizing the need for careful assessment and physical validation during surgery. Imaging examples showed potential instances of Chiari type II and craniovertebral instability-related complications such syringomyelia and herniation of the cerebellar Specific surgical techniques amvgdala. atlantoaxial facetal fixation and fixation methods for basilar invagination were discussed in various studies, highlighting the challenges and strategies for stabilization in these conditions. [10]. According to Atul Goel, the preferred treatment for basilar invagination is typically atlantoaxial joint fixation or distraction. [11].

When evaluating occipital-atlantoaxial movements. crucial measurements include the basion-atlas interval, the horizontal section of the clivus, the anterior arch of the atlas, and the dens interval in the including its angle. Additionally, relationship between the clivus angle and the atlas, or the clivus-atlas angle, should be considered. [16]. CT scans of the atlantoaxial region allow measurements in both sagittal and coronal slices. Lateral radiographs indicate flexion and extension, aiding in the identification and evaluation of craniovertebral junction (CVI) stability using magnetic resonance imaging (MRI) during these movements. Instability may manifest in various symptoms such as atlantoaxial and atlanto-occipital ligament loss, neck pain, restricted neck muscles, and sensory or motor abnormalities. [17]. Patients with connective tissue diseases may experience spasticity, involuntary contractures of cervical and thoracic muscles, and craniocervical instability. Postoperative discomfort can be managed with painkillers, and drugs like tizanidine or baclofen may assist in pain management. It's important to note that individuals diagnosed with postural orthostatic tachycardia syndrome (POTS) should avoid haloperidol. [18].

Trauma is associated with connective tissue disorders and congenital abnormalities of the craniocervical junction, leading to craniocervical instability. [24]. Symptoms can be effectively managed through postural cues, stabilizing exercises, and manipulative axial traction techniques. [25]. Halo immobilization, followed by regular lateral cervical radiographs, may be employed initially. If the craniocervical alignment is unsatisfactory after a week, readjustment of the halo device under fluoroscopic supervision might be necessary. [26]. Basic radiography serves as a baseline for occipitoatlanto or atlantoaxial joint instability assessment. [27]. Craniometric studies indicate basilar invagination in healthy individuals and those with Chiari malformation, highlighting changes in the clivus canal angle, craniocervical kyphosis, and thickening of the lordotic cervical column. [28]. The CVJ contributes significantly to cervical spine function, enabling 50% axial rotation and 25% flexion and extension of the neck. [29]. Maintaining sagittal balance and realigning the cervical spine may impact postoperative clinical outcomes positively. [30]. Clinical arrest testing aids in identifying precise craniocervical ligament instability and hypermobility. [31]. Computed tomography angiography is crucial for surgical planning to detect vertebral artery injuries, minimize risks, and identify vascular anomalies early. [32]. Endoscopic endonasal techniques offer a highly adjustable, ventrally situated, and steep learning curve approach for performing safe decompression in the cervicomedullary region. [33].

Variability exists in basilar processes concerning shapes and sizes in relation to the atlas and its axis. [34]. Anterior techniques employing anterior odontoid screws contrast with posterior procedures using anchor rods, atlantoaxial fixation, or occipitocervical fixation with screws. [35].

A comprehensive understanding of anatomy and biomechanics is pivotal in evaluating diseased processes in the affected region. Patients without pre-existing instability or dislocation and in good health pre-surgery might qualify for transoral surgery. [36].

#### **LIMITATIONS**

Study Selection Limitations: Despite the use of specific inclusion and exclusion criteria, the selection of studies might be subject to some degree of subjectivity, and some relevant studies might have been unintentionally excluded.

Risk of Bias in Included Research: Taking in a certain number of studies for the review might carry a risk of bias, especially if these studies have methodological limitations such as selection, reporting, or confounding biases.

Limitations in Outcome Assessment: The review might not provide a comprehensive overview of all possible outcomes or long-term complications related to various craniovertebral junction stabilization techniques.

Limitations in Formulating Recommendations: Final recommendations or conclusions might be influenced by the limited availability of data or lack of general consensus within the medical and surgical field.

#### **CONCLUSION**

The management of atlantoaxial instability remains a subject of significant debate, especially concerning its implications in genetic connective tissue disorders. Craniovertebral junction instability presents a complex challenge that demands careful

consideration. Key recommendations arising from these discussions include:

- 1. Prioritize key stabilization techniques, especially at the C1-C2 level, in cases of craniovertebral junction instability.
- Consider the use of benzodiazepines for muscular relaxation and other opioid medications for effective postoperative management.
- 3. While a majority lean towards transpedicular pedicle screws, individual preferences vary considerably.
- 4. Techniques advocated by Harms and Atul Goel are favored due to their requirement of only 22 degrees.
- Consider utilizing odontoid screws for fixation and exploring posterior procedures involving anchor rods, atlantoaxial fixation, or occipitocervical fixation using screws. Additionally, computed tomography angiography and Halo immobilization can offer valuable insights and aid in postoperative care.

In the management landscape for atlantoaxial instability is multifaceted, demanding a nuanced approach tailored to individual patient needs. Further research and consensus-building efforts are essential to refine treatment strategies and enhance patient outcomes in this challenging area of spinal pathology.

#### **Declarations**

The authors have no conflict of interest to declare.

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No part of this study was published in any matter previously.

All authors have read and approved the final manuscript.

Ethical approval No applicable

Acknowledge No

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