Original Paper

Pediatric Neurosurgery

Pediatr Neurosurg 2019;54:12–20
DOI: 10.1159/000495788

Received: March 26, 2018
Accepted after revision: November 23, 2018
Published online: January 24, 2019

Dynamic MRI in the Evaluation of Atlantoaxial Stability in Pediatric Down Syndrome Patients

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Keywords
Down syndrome · Congenital disorder · Craniocervical instability · Management · Dynamic MRI

Abstract
Background/Aims: Down syndrome is the most common inherited disorder. Some patients develop atlantoaxial instability. Existing screening guidelines were developed prior to availability of MRI. We present predictors for deficit using dynamic MRI of the craniocervical junction. ***Methods:*** A retrospective review of Down syndrome patients from 2001 to 2015 was carried out. Patients were considered symptomatic if they had clinical deficits or signal change on MRI. Measurements were taken at the atlantoaxial junction and structural abnormalities noted. Analysis was performed with SPSS. ***Results:*** A total of 36 patients were included. Patients averaged 93 months of age with a follow-up of 57 months. No asymptomatic patients developed myelopathy during follow-up. During dynamic imaging, symptomatic patients had greater changes in space available for the cord (SAC) (5.2 vs. 2.7 mm; $p < 0.001$) and atlantodental interval (ADI) (2.8 vs. 1.3 mm; $p = 0.04$). These patients were also more likely to have a bony anomaly (50 vs. 13%; $p = 0.03$). ***Conclusion:*** This study characterizes the range of motion seen on dynamic MRI and provides parameters that can be used to distinguish patients at risk for neurologic injury. Changes greater than 3 mm in ADI or 5 mm in SAC during dynamic MRI or any bony abnormality warrants further investigation. Patients without these features may be able to avoid an unnecessary intervention.

Introduction

Down syndrome is the most common inherited disorder, reaching a prevalence of 1.5/1,000. A proportion of patients develop neurologic deficit owing to pathologic changes at the atlantoaxial junction. These changes may result in direct compression of neurologic structures or recurrent injury from repetitive movement. While screening guidelines for instability exist, these were developed in an era of plain radiograph and without direct imaging of the neurologic structures. Here, we attempt to better quantify the normal movement parameters seen in children with Down syndrome using dynamic and static MRI, as well as to identify radiographic predictors for neurologic deficit or instability.

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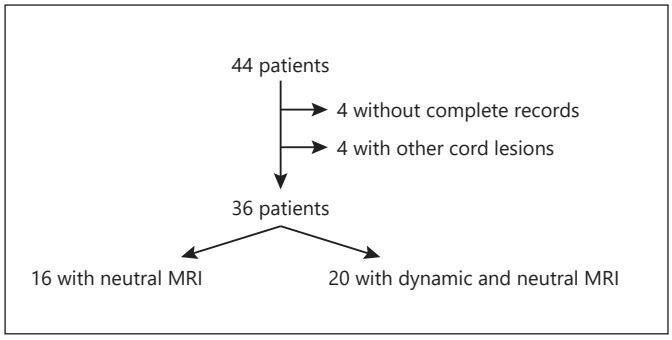


Fig. 1. Patient selection.

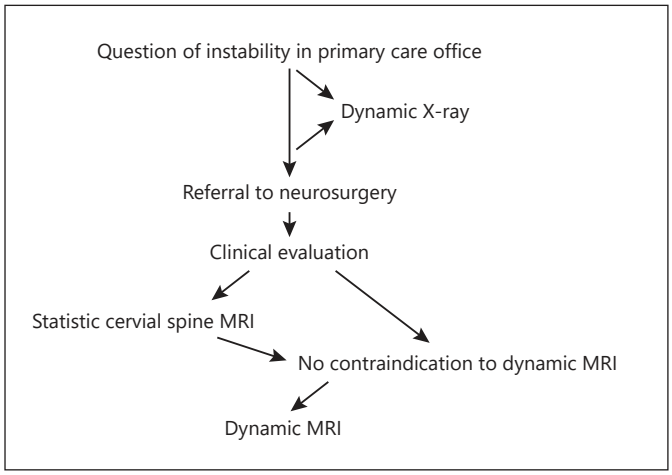


Fig. 2. Referral for dynamic MRI algorithm.

Methods

Approval for this study was obtained from the institutional research ethics board. All patients with Down syndrome referred to the Children's Hospital Los Angeles (CHLA) neurosurgery division from 2001 to 2015 were reviewed. Patients were included for study if they had dynamic or static craniocervical MRI studies. Only patients with complete radiographic and clinical records with at least 1 year of follow-up were included for study. Some patients also had plain radiographs – these images were analyzed separately. Data collection was done in a blinded fashion where patient charts and imaging were evaluated independently in separate data sets. Only during data analysis were datasets merged. Patients being evaluated for other spinal cord lesions remote from the cervical spine such as lumbosacral lipomas or low-lying conus were excluded from the study (Fig. 1). Patients were considered symptomatic if they had neurologic deficit related to cord/brainstem compression (i.e., cranial nerve deficit, paresthesias, motor weakness, hyper reflexia, proprioceptive deficit, myelopathy) that was detected in the neurosurgical clinic or if they had a signal change at the craniocervical junction (defined as a region of hyperintensity within the cord parenchyma seen on T2-weighted images). Patients were classified as asymptomatic if they had no evidence of signal change and no neurologic deficits.

Obtaining Dynamic MRI

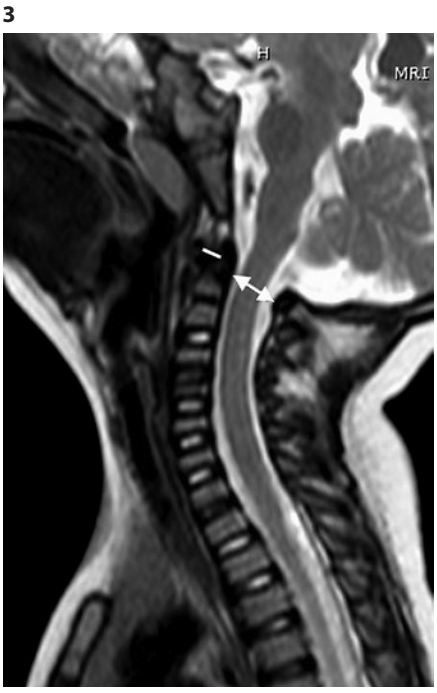
Patients were referred from their primary care providers due to clinical instability (i.e., gait change, head tilt, etc.). Not all patients had radiographic evaluation prior to referral and instability. Patients presenting for evaluation who were overtly unstable (i.e., in a hard collar or after significant trauma) only had static MRI and did not undergo dynamic MRI. An initial baseline static MRI without contrast was obtained for patients. If there were no overt radiographic contraindications to dynamic imaging seen, a qualified neurosurgical practitioner (physician assistant or neurosurgical fellow) would then reposition the patients in flexion, followed by extension positioning. The head and neck were supported using foam wedges slotted behind the patient's head and shoulders. Care was taken to ensure that extremes of flexion and extension were avoided, and repositioning replicated what might be seen in a normal, physiologic setting. Imaging for patients was done under non-intubated or intubated sedation according to patient compliance with the scan and the discretion of the anesthesiologists. No patients developed new neurologic deficits after the imaging study. No patients had neuromonitoring during their studies (Fig. 2).

Measurements

Patient MRIs were evaluated using standardized measurements. Cervical spine images were evaluated in neutral, flexed, and extended positions (when available). Movement across C1 and C2 was determined by measuring the atlantodental interval (ADI) and space available for the cord (SAC) in the midsagittal plane. Cervical angle (CA), clival axial angle (CXA), the maximal and minimal cord diameters in the cervical spine, the maximal and minimal cervical canal diameters, and the levels of the maximal and minimal cord diameters were also measured in the midsagittal plane (Fig. 3, 4). Measurements were taken from radiology reports when available and were repeated or carried out by the first author (A.T.). In cases when there was a discrepancy between the author's and the reported measurements, then the radiologists' measurements were used. The presence of any bony abnormality at the craniocervical junction (i.e., occiput to C2) was also recorded (i.e., incomplete atlas, nonsegmentation of the atlas, dens abnormalities). Data analysis was performed using SPSS Version 22. A p value <0.05 was considered significant.

Results

A total of 44 patients with Down syndrome were seen between January 2001 and January 2015 with imaging for CNS lesions. Of these, 4 were excluded for incomplete records. and 4 additional patients were excluded for cord abnormalities (i.e., low-lying conus). Of the 36 remaining patients, 20 had dynamic and neutral-position MRI for analysis while 16 had only neutral imaging (Fig. 1). Patients were 93 months of age on average at presentation



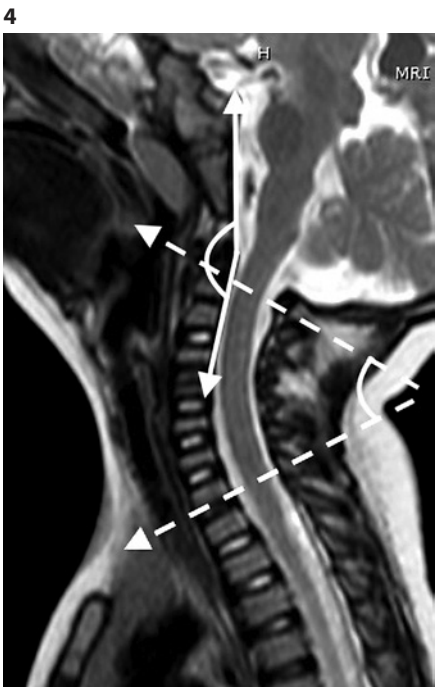


Fig. 3. Measurement of ADI and SAC. The white line measures the ADI – from the posterior aspect of C1 to the front of the dens. The double-headed arrow measures the SAC – from the posterior aspect of the dens to the anterior aspect of the arch of C1.

Fig. 4. Measurement of CXA and CA. The angle between the solid arrows measures the CXA – the angle between the posterior aspect of the clivus and the posterior aspect of the dens. The angle between the hatched arrows measures the CA – the angle between the bottom of C1 and the bottom of C7.

with a range of 17–240 months; 19 of the 36 patients were male. Follow-up ranged from 12 to 168 months with an average of 57 months. No initially asymptomatic patients developed new deficits during follow-up; 2 patients presented with myelopathy, while 4 patients were found to have a signal change without overt neurologic symptoms of neuraxis compression (Table 1). No patients had syrinx or signal change elsewhere in the neuraxis.

Table 1. Study demographics

	Asymptomatic (n = 30)	Symptomatic (n = 6)
Male sex, n	17	2
Mean age at presentation, months	95	85
Mean follow-up, months	59.4	39.6

Range of Motion in Asymptomatic Patients

In asymptomatic patients, the average minimal cord diameter in the neutral position was 6.1 mm while SAC was 13.8 mm. The average minimal canal diameter was 10.1 mm. Mean neutral ADI was 3.0 mm. CXA was 151° while CA was 42° in the neutral position. On dynamic imaging, the average minimal cervical canal diameter changed from 10.9 mm in flexion to 9.9 mm in extension with a mean change of 0.9 mm. The average ADI changed from 3.3 to 2.3 mm during flexion to extension with a mean change of 1.3 mm (0.1–3.2 mm). CXA changed from 140° in flexion to 154° in extension with a mean change of 15° (1–34°). CA ranged from 13.2 to 56.4° during flexion to extension with a mean change of 43° (15–76°). Complete results are reported in Tables 2–5.

Predictors of Myelopathy or Signal Change with MRI

In contrast, symptomatic patients had a smaller minimal cord diameter (4.6 vs. 6.1 mm; $p = 0.002$), narrower SAC (9.4 vs. 13.8 mm; $p = 0.003$), and larger ADI (4.4 vs. 3.0 mm; $p = 0.01$) at rest. CXA approached but was not significantly less than in asymptomatic patients (141 vs. 151°; $p = 0.08$). On dynamic imaging, SAC decreased significantly in flexion (6.9 vs. 12.0 mm; $p = 0.008$) but reduced in extension (12.1 vs. 12.9 mm; $p = 0.58$). Furthermore, the change in SAC (5.2 vs. 2.7 mm; $p < 0.001$) as well as ADI (2.8 vs. 1.3 mm; $p = 0.04$) between flexion and extension in individual patients was strongly predictive, as was the presence of bony abnormality at the craniocervical junction (50 vs. 13%; $p = 0.03$) (Table 6).

Correlation of MRI to Radiograph

In total, 13 patients had plain radiographs that were available for comparison to MRI. ADI, CXA, and CA were compared (Table 7). SAC was not reliably measur-

able on the majority of radiographs and was excluded from analysis. In a neutral position, correlation between MRI and radiograph was worst for CA (r = –0.11) and best for CXA (r = 0.86). On dynamic imaging, correlation was best for CXA (0.95) and least accurate for ADI (–0.06) (Table 7).

Prediction of Myelopathy or Signal Change with Radiograph

Overall, 20 asymptomatic and 4 symptomatic patients had both MRI and radiograph available for comparison. None of ADI, CXA, or CA on dynamic radiograph were able to differentiate symptomatic patients from their asymptomatic peers (Table 8).

Discussion

Radiographic and Clinical Instability

Patients with Down syndrome face an increased incidence of radiographic instability, approaching 30% in some studies [1–5, 6, 7]. The actual number of symptomatic patients varies, however, but may be as few as 1.5% depending on how symptomatology is defined [7, 8, 9–13]. Examination of Down syndrome patients is challenging owing to varying degrees of cognitive impairment or existing physical disability that mask subtle changes until function is severely compromised. Previous publications have attempted to identify reliable markers using dynamic X-rays or CT for radiographically significant instability; clinical correlation, however, is inconsistent at best [7, 8, 13]. Furthermore, no published parameters indicating instability currently exist for dynamic MRI in Down syndrome patients. Given the advantages of MRI over other imaging modalities, including avoiding repeated ionizing radiation exposure and direct imaging of the neuraxis under load, we would anticipate that this imaging modality will become more widely adopted over time. Thus, it is critical to establish a set of normative parameters that may be measured on dynamic MRI.

As seen in this study, we observed poor correlation for dynamic radiographs to both symptomatic patients and to the dynamic MRIs performed. One explanation for this discrepancy may be the varying techniques that outside centers may utilize in performing dynamic radiography. In comparison, all dynamic MRIs were performed within our own institution using a consistent protocol. Given the limitations of clinical examination and the poor outcome associated with latent neurological injury, dynamic MRI

Table 2. Measured patient parameters in neutral position

	Asymptomatic	Symptomatic	*p* value
ADI, mm	**3**	**4.4**	**0.01**
SAC, mm	**14**	**9.4**	**0.003**
Minimal cord diameter, mm	**6.3**	**4.6**	**0.002**
Minimal canal diameter, mm	10.1	11	0.38
CA, degrees	42.1	27.2	0.15
CXA, degrees	151	141	0.08
Patients with bony abnormality, %	**13.3**	**50**	**0.03**

Values in bold indicate significant difference between symptomatic and asymptomatic patients.

Table 3. Measured patient parameters in flexed position

	Asymptomatic	Symptomatic	*p* value
ADI, mm	3.3	4.9	0.08
SAC, mm	**12**	**6.9**	**0.008**
Minimal cord diameter, mm	6.1	4.5	0.05
Minimal canal diameter, mm	10.9	10.3	0.66
CA, degrees	13.2	–12	0.05
CXA, degrees	140	133	0.51

Values in bold indicate significant difference between symptomatic and asymptomatic patients.

Table 4. Measured patient parameters in extended position

	Asymptomatic	Symptomatic	*p* value
ADI, mm	2.3	2.1	0.82
SAC, mm	12.9	11.6	0.58
Minimal cord diameter, mm	6.3	6.4	0.91
Minimal canal diameter, mm	10	10.8	0.64
CA, degrees	56.4	52.5	0.77
CXA, degrees	154	150.5	0.71

Table 5. Measured changes in patient parameters from flexion to extension

	Asymptomatic	Symptomatic	*p* value
ADI, mm	**1.3**	**2.8**	**0.04**
SAC, mm	**1.2**	**5.2**	**<0.0001**
Minimal cord diameter, mm	**0.17**	**1.9**	**<0.0001**
Minimal canal diameter, mm	0.9	0.5	0.24
CA, degrees	43.2	64.5	0.12
CXA, degrees	14.8	17.5	0.66

Values in bold indicate significant difference between symptomatic and asymptomatic patients.

Table 6. Summary of significant predictors for instability/neurologic deficit

	Asymptomatic	Symptomatic	*p* value
Neutral position ADI, mm	3	4.4	0.01
Neutral position SAC, mm	14	9.4	0.003
Change in ADI from flexion to extension, mm	1.3	2.8	0.04
Change in SAC from flexion to extension, mm	1.2	5.2	<0.0001
Patients with bony abnormality, %	13.3	50	0.03

Table 7. Correlation of plain radiograph to MRI

Position	MRI	Plain radiography	Correlation, *r*
Neutral			
Mean ADI, mm	3.3	2.7	–0.05
Mean CXA, degrees	150	159	0.86
Mean CA, degrees	21	36	–0.11
Flexion			
Mean ADI, mm	3.2	3.7	0.56
Mean CXA, degrees	139	145	0.39
Mean CA, degrees	12	–3	0.51
Extension			
Mean ADI, mm	2	2.6	–0.02
Mean CXA, degrees	153	170	0.39
Mean CA, degrees	56	55	0.15
Change from flexion to extension			
Mean ADI, mm	1	1	0.06
Mean CXA, degrees	25	36	0.95
Mean CA, degrees	44	43	0.6

Table 8. Prediction of symptomatic patients using plain radiograph

Parameter	Asymptomatic	Symptomatic	*p* value
Flexion			
ADI, mm	3.5	4.2	0.58
CA, degrees	–3.25	–12.5	0.36
CXA, degrees	145	148	0.76
Extension			
ADI, mm	2.3	3.4	0.24
CA, degrees	56	76	0.15
CXA, degrees	170	173	0.63
Change from flexion to extension			
ADI, mm	1.3	1.1	0.64
CA, degrees	60	89	0.13
CXA, degrees	42	74	0.35

allows for direct determination of whether neuraxis injury is occurring.

This modality has been used in adult populations to characterize pathologies of the cervical spine that may not be immediately apparent in a neutral supine position. Including these views increases the detection or exclusion of true instability [2, 6, 14–16]. In this study, we selected what we felt to be definable indicators of neuraxis injury using parameters on dynamic MRI. These measurements were consistently measurable by the authors on a dynamic MRI. While other measurements are also possible, the authors of this publication specifically sought out measures that could be reasonably taken in the office setting by a trained neurosurgeon and did not require significant additional training to interpret.

Etiology of Instability

Previous publications have identified soft tissue changes including decreased paraxial muscle tone and increased ligamentous laxity in patients with Down syndrome [4, 7, 8, 11]. More recently, abnormally flattened articulations between the occipital condyles and atlas lateral masses have also been identified, increasing the degrees of movement at the craniocervical junction [7, 17–20]. Furthermore, as we saw in our study, there is also an increased incidence of bony abnormalities in the atlas (e.g., nonsegmentation or incomplete arch) and axis (e.g., os odontoideum) [1, 7, 8, 11, 19]. The combination of these abnormalities allows abnormal movement across the atlantoaxial junction or may cause excessive motion across a single level resulting in potential injury to the neurologic structures. None in isolation are definitively predictive for the development of symptomatology, although the presence of os odontoideum has been suggested as an indication for more in-depth investigation [7, 11, 17, 19]. From our study, we identified several predictors for instability that suggested movement across the atlantoaxial junction (i.e., ADI, SAC). While instability at other areas of the craniocervical junction and cervical spine are possible, we suspect that the relatively low numbers of symptomatic patients in this study do not encompass the entire spectrum of dynamic craniocervical pathology in patients with Down syndrome.

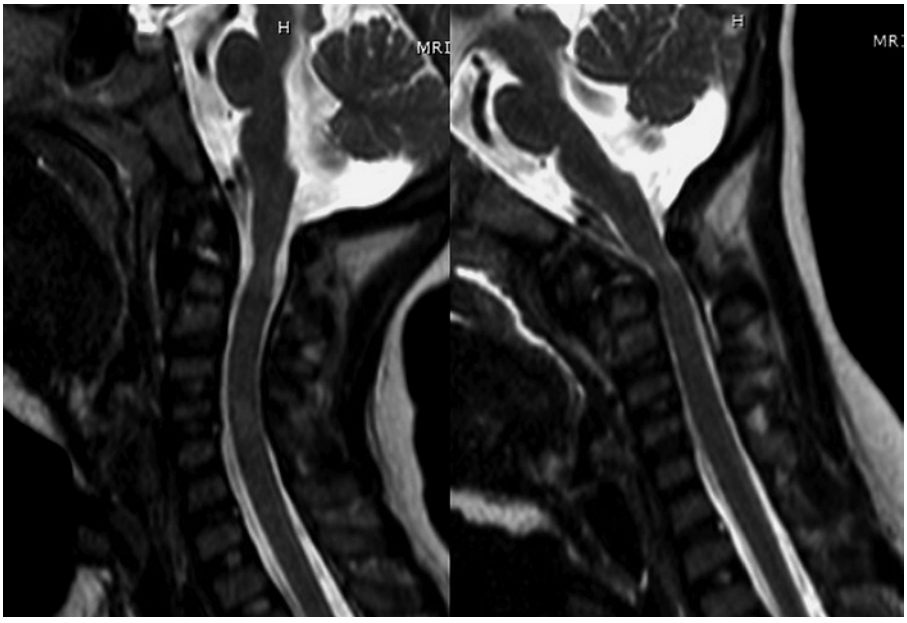


Fig. 5. Example of Instability on dynamic imaging. The left-sided image is a T2-weighted MRI in the sagittal plane with the head in a neutral position. The right-sided image is the head now in flexion. Note the movement of C1, dens fracture, and compression of the neuraxis.

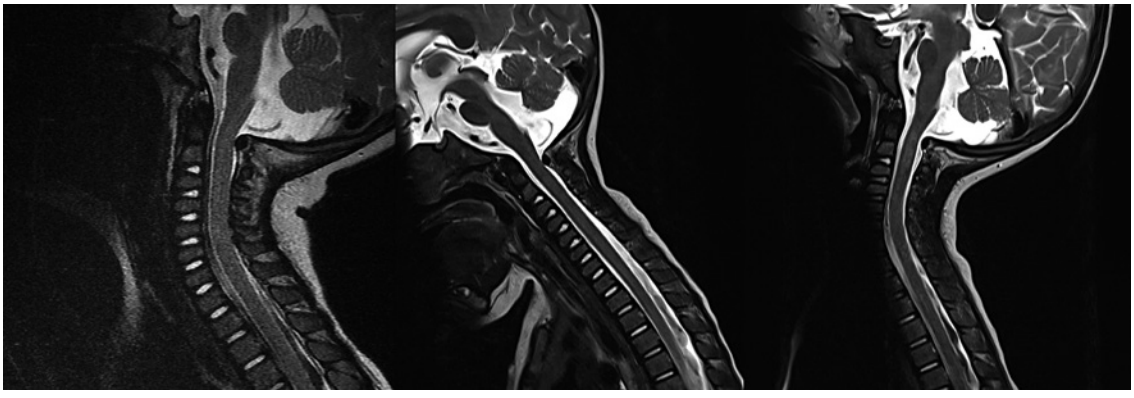


Fig. 6. Example of stability on dynamic imaging. The left-sided figure is a static T2-weighted MRI in the sagittal plane. Initial review of this imaging was concerning for a hypoplastic arch of C1 resulting in upper cervical cord indentation. On dynamic imaging in flexion (center) and extension (right), the cord is seen to actually have reasonable space surrounding the cord and no significant dynamic instability or movement requiring operative intervention.

Etiology of Neurologic Deficit

Despite systemic changes in anatomy, the vast majority of Down syndrome patients do not develop deficits. Thus, not all exaggeration of movement across the atlantoaxial junction and upper cervical spine is clinically significant. From this study, we found that the mobility of the subaxial spine in the sagittal plane was not significantly different between symptomatic and asymptomatic patients, downplaying the potential role that subaxial instability may play in causing deficit. In this study, we observed that most symptomatic patients had dynamic compression that was apparent only on flexion and occurring across the atlantoaxial junction, similar to findings from other centers [6, 15] (Fig. 5). Even in patients without Down syndrome, the craniocervical junction is an area with a unique anatomy that predisposes it to certain patterns of injury [3, 6, 8, 17–20]. Neonates and infants are particularly prone to injury in this region owing to their disproportionately large head and developing neck musculature [6, 17, 19]. While most children eventually outgrow this propensity, Down syndrome patients remain persistently at risk for the reasons outlined above.

Utility of Dynamic MRI

Current American Association of Pediatrics guidelines do not recommend routine radiographic screening of asymptomatic Down syndrome patients, which is reasonable given the additional time and resources required without clear benefit [5]. In patients with a question of instability, in our experience plain radiograph has been inadequate in identifying instability. In our series, while some features on static MRI alone correlated to instability, the addition of dynamic MRI was valuable in identifying patients who did not need surgery. In this subset, static images suggested the possibility of cord impingement seen as narrowing of the cord parenchyma at the atlantoaxial junction, but without extrinsic compression. When dynamic studies were added to the evaluation, these patients were found to have no cord impingement associated with movement and cord deformation was not indicative of instability (Fig. 6). It is unclear why focal cord narrowing occurs in some of these patients, but anecdotally the authors have observed it in other conditions as well, including patients with disc herniation and presumed canal stenosis. In patients where no overt anatomic compression is occurring, then the narrowing probably represents an incidental congenital finding. It is arguable that in these patients, the addition of dynamic imaging is most valuable given its ability to exclude a potentially unnecessary intervention.

Who Should Not Undergo Dynamic Imaging?

The role of dynamic MRI in the evaluation of patients with Down syndrome remains controversial and not well defined. While some centers have anecdotally developed protocols for its use, these procedures are neither standardized nor evidence based. We fully recognize the challenges that are associated with obtaining dynamic MRI in this population including the potential for iatrogenic injury associated by placing sedated patients in nonneutral positions during imaging. We do not advocate that every patient presenting to a neurosurgical practice undergo dynamic MRI as part of the standard work-up. Instead, patients should be clinically evaluated for instability and neurologic deficit; they should only undergo dynamic MRI if indicated and safe for the patient. Patients with potential myelopathy but no overt compression on static images may benefit from dynamic imaging as it determines whether dynamic compression of the neurologic structures exist. In cases where static imaging demonstrates obvious compression that explains the patient symptomatology, dynamic imaging is not likely to provide further information and may be omitted.

Most of our patients were ambulatory; even those that were not were able to support their cranium independently, thus demonstrating that they were tolerating physiologic loading on a day-to-day basis. Patients with reason for overt instability (e.g., major cervical trauma) or in a hard cervical orthosis were precluded, and we would advocate that these patients do not have dynamic imaging. From our experience, it is unnecessary to place the head and upper cervical spine into the extremes of positioning that risk potential spine injury in order to identify instability.

Alternative Imaging Considerations

We recognize that other centers also may also utilize alternative means of dynamic imaging. In this study, we were able to compare correlation of dynamic radiography to symptomatic patients and found a poor correlation. Other centers have utilized dynamic CT to improve prediction of instability. From an institutional practice perspective, we have attempted to minimize the use of CT in the pediatric population. As a result, the vast majority of our patients did not undergo CT studies of their brain or cervical spine as part of their routine evaluation unless delineation of the bony was otherwise indicated (e.g., presurgical planning).

Formal Recommendations

The lack of consistent normative values for dynamic MRI makes interpretation challenging for practitioners. From this study, we can make the following observations – average CXA in Down syndrome patients of 140° in flexion to 154° in extension is not associated with an increased incidence of neurologic injury. Similarly, an average CA of 13° in flexion to 56° in extension represents a normal range of motion in this population. When screening for instability, SAC and ADI were most reliable in predicting clinically significant instability. A neutral-posture SAC of greater than 14 mm was unlikely to be associated with instability while 9 mm or less was strongly associated with neuraxis compromise and treatment should be considered. If a neutral-position SAC is between 9 and 14 mm, further investigation should be considered including dynamic imaging and direct imaging of the neuraxis in the form of MRI to look for evidence of injury. Any change in dynamic imaging in the SAC of 5 mm or more between flexion and extension is associated with neuraxis compromise and warrants evaluation and treatment. In addition, a neutral-position ADI of 4 mm or more was associated with neuraxis injury while 3 mm or less was not associated with significant instability. Given the small

but significant differences in neutral ADI associated with neuraxis injury, we would suggest further investigation in patients with neutral-posture ADI greater than 3 mm in the form of dynamic imaging. A change in ADI greater than 3 mm on flexion and extension views should warrant further investigation and or treatment.

Limitations

This is an initial study and additional patients are required to validate our findings, as well as to further refine the parameters that we have set out. The small population size in addition to relative rarity of clinical instability limits our ability to evaluate for pathologic movement occurring outside the atlantoaxial junction. The measurements in this study have been obtained using our MRI protocols, and replication at other centers by other observers will allow the development of individual protocols that are best suited to regional differences. In addition, the patients in this study were referred to CHLA neurosurgery for evaluation of possible instability, either radiographically or clinically, and are not necessarily representative of the overall Down syndrome population. Furthermore, very few of the patients in this study have had follow-up extending into adulthood or beyond, and the contribution of degenerative changes that occur with aging is not well known.

Conclusion

This study establishes a preliminary normative range of parameters for the atlantoaxial junction and subaxial spine in patients with Down syndrome, as well as objective measurements that identify patients at risk for neurologic compromise. An SAC less than 9 mm or ADI greater than 4 mm on neutral MRI, changes in ADI greater than 3 mm or SAC greater than 5 mm on dynamic MRI, or the presence of any bony abnormality warrant investigation and/or treatment. Patients without these features may be able to avoid an unnecessary intervention. In appropriately selected Down syndrome patients, dynamic MRI is a safe and valuable adjunct that may contribute significant information to patient management.

Statement of Ethics

Approval for this study was obtained from the institutional research ethics board.

Disclosure Statement

On behalf of all authors, the corresponding author states that there is no conflict of interest.

Funding Sources

No additional internal or external funding was obtained for this study.

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