Upper Cervical Fusion in Children with Morquio Syndrome

Intermediate to Long-Term Results

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Background: Paraplegia or death secondary to upper cervical spine instability and spinal cord compression are known consequences of Morquio syndrome. Decompression and fusion of the upper cervical spine are indicated to treat spinal cord compression. The purpose of this study was to report the intermediate to long-term results of upper cervical spine fusion in children with Morquio syndrome.

Methods: Twenty patients (nine female and eleven male) with Morquio syndrome who underwent upper cervical spine fusion at a mean age of sixty-three months were retrospectively analyzed with use of hospital records. Radiographic and clinical results were reported.

Results: The average follow-up period was eight years and ten months. Fusion was achieved in all patients except one; this patient underwent a revision with transarticular C1-C2 screw fixation. Seven patients developed symptomatic instability below the fusion mass that required extension of fusion to lower levels at a mean of ninety-one months after the initial operation. Two patients required decompression and fusion of a site other than the upper cervical spine. Asymptomatic cervicothoracic and thoracolumbar kyphosis was prevalent among our patients. All patients were neurologically stable at the time of the latest follow-up visit.

Conclusions: Upper cervical spine fusion provides reliable fusion and a stable neural outcome in patients with Morquio syndrome. However, distal junctional instability is a major problem at long-term follow-up. Kyphotic deformity of the cervicothoracic and thoracolumbar junction may be present in a large number of patients with Morquio syndrome and evaluation for spinal stenosis at these levels should also be considered.

Level of Evidence: Therapeutic Level IV. See Instructions for Authors for a complete description of levels of evidence.

Morquio syndrome is the type of mucopolysaccharidosis (type IV) with the most frequent skeletal consequences. In addition to extremity alignment abnormalities, the natural progression of the disease may lead to quadriplegia and sudden death secondary to upper cervical spine instability and cord compression[1-3]. Specifically, children with Morquio syndrome have odontoid hypoplasia, ligamentous laxity, and extradural mucopolysaccharide deposition anterior to the spinal cord at the C1 level that can result in atlantoaxial subluxation, stenosis, and cervical myelopathy. The extradural mucopolysaccharide deposition can accentuate cord compression, and thus, the magnitude of cord compression could be more than expected on the basis of standard radiographs[2,4,5]. The outcome of disease progression led several authors to recommend fusion of the upper cervical spine once instability is demonstrated[2,4-8].

Several studies have shown the results of upper cervical fusion in patients with Morquio syndrome; however, long-term results and complications of upper cervical fusion in this population have not been well documented. The purpose of this study is to show the intermediate to long-term clinical and radiographic outcomes of upper cervical spine fusion in children with Morquio syndrome.

Disclosure: None of the authors received payments or services, either directly or indirectly (i.e., via his or her institution), from a third party in support of any aspect of this work. None of the authors, or their institution(s), have had any financial relationship, in the thirty-six months prior to submission of this work, with any entity in the biomedical arena that could be perceived to influence or have the potential to influence what is written in this work. Also, no author has had any other relationships, or has engaged in any other activities, that could be perceived to influence or have the potential to influence what is written in this work. The complete **Disclosures of Potential Conflicts of Interest** submitted by authors are always provided with the online version of the article.

TABLE I The Preoperative Imaging Findings

Patient No.	Space Available for the Cord in Flexion* (mm)	Space Available for the Cord in Extension† (mm)	Sagittal Cord Diameter‡ (mm)	Signal Change	Cord Compression	Cervicothoracic Kyphosis	Thoracolumbar Kyphosis
3	8.2	12.6	6.5	Yes	Yes	Yes	Yes
4	8.7	12	5.9	Yes	Yes	Yes	Yes
6	9.4	11.2	6.3	No	Yes	No	No
7	9	13	NA§	NA	NA	Yes	No
8	14	17	8.3	Yes	Yes	Yes	No
9	10.1	13.3	6.6	Yes	Yes	No	Yes
11	10.3	12.9	8.6	No	Yes	No	Yes
12	12	16	8.9	No	Yes	No	Yes
15	8	10	5.6	Yes	Yes	No	Yes
20	10.2	15	7	No	Yes	Yes	No

*The mean space available for the cord in flexion was 10 mm. †The mean space available for the cord in extension was 13.3 mm. ‡The mean sagittal cord diameter was 7 mm. §N/A = not available. Patient No. 7 did not have MRI.

Materials and Methods

After institutional review board approval, we searched the medical records for patients with a diagnosis of Morquio syndrome. A total of thirty-six patients with this diagnosis from 1979 to 2007 were identified. The inclusion criteria were a confirmed diagnosis of Morquio syndrome, surgical fusion of the upper cervical spine, and a minimum of twenty-four months of radiographic follow-up.

Twenty-seven of the thirty-six patients underwent cervical fusions either at our institution or at an outside facility. Twenty-five patients underwent only upper cervical fusions. Two patients underwent upper cervical fusion as well as decompression and fusion for spinal stenosis at a location unrelated to the cervical spine. None of the patients underwent spinal fusion only for thoracic or lumbar deformity. Data for more than twenty-four months of follow-up were available for twenty-one patients, and twenty patients satisfied the inclusion criteria. Of these twenty patients, five had C1-C2 fusion, one had occiput-C3 fusion, and fourteen had occiput-C2 posterior spinal fusions. The fusion levels were chosen according to the level of instability and cord compression. In cases in which posterior elements of C1 were incompetent for fixation, or were removed for decompression, fusion was done between the occiput and C2 unless stenosis and/or instability involved lower levels. Twelve of the twenty patients had the index fusion surgery at an outside institution. The eight patients who underwent operations at our institution and two of the twelve patients who underwent operations elsewhere had preoperative and postoperative radiographs at scheduled clinic visits. The remaining ten patients only had postoperative follow-up radiographs in our records.

The posterior atlantodens interval (space available for the cord) was measured preoperatively in flexion and extension views of lateral cervical spine radiographs. Preoperative magnetic resonance imaging (MRI) and computed tomographic (CT) scans were evaluated when available. The diameter of the dura was measured between the odontoid and the posterior arch of the atlas on MRI sagittal views to correlate with the measurements of space available for the cord on radiographs.

Anesthesia

There are multiple case reports in the anesthesiology literature addressing the specific anesthetic difficulties and how to manage the airway in patients with Morquio syndrome. Jones and Croley[9] noted that the three major problems were difficulty in intubation because of the deformity and redundant pharyngeal mucosa, chronic pulmonary disease due to chest deformity and superinfection, and inadvisability of manipulating the neck because of vertebral anomalies and possibility of atlantoaxial subluxation. Tzanova et al.[10] recommended fiber-optic-guided nasotracheal intubation, which does not require repositioning of the head, in patients with Morquio syndrome. McLaughlin et al.[11] recently reported that, in addition to cervical instability, bulky pharyngeal tissues (due to the deposition of mucopolysaccharides in the oropharynx, floor of the mouth, epiglottis, aryepiglottic folds, and macroglossia) mandate the use of a smaller endotracheal tube. Also, a prominent maxilla, limited mouth opening, and short neck make safe direct laryngoscopy difficult. McLaughlin et al. advised preoperative awake fiber-optic airway examination. Theroux et al.[12] preferred using the Glidescope while performing intubation on children with Morquio syndrome. In these children, airway abnormalities include a tortuous appearance of the trachea and bronchi as a result of abnormalities in hyaline cartilage and deposits of glycosaminoglycans.

Postoperative Care

All patients, except one with bilateral transarticular screw fixation, were immobilized in a halo vest for three months. After three months, the halo vest was removed in the clinic, and the patients used a cervicothoracic orthosis for another six to twelve weeks. Patients were allowed to return to normal activity at six months.

Source of Funding

No funding was received for this study.

Results

A total of twenty patients met the inclusion criteria (see Appendix). The average follow-up period was 106 months (range, twenty-six to 192 months). The average patient age at initial fusion surgery was sixty-three months (range, twenty-two to 179 months). Of the twenty patients, all but one achieved fusion of the operated levels after initial surgery.

We were able to report the index fusion indications only for the patients who underwent the initial surgery at our institution. The indications included progressive instability in three patients, cord compression along with instability in three patients, myelopathy in one patient, and paralysis in one patient. These eight patients had MRI scans, and six of them showed signal changes in the spinal cord at the unstable level.

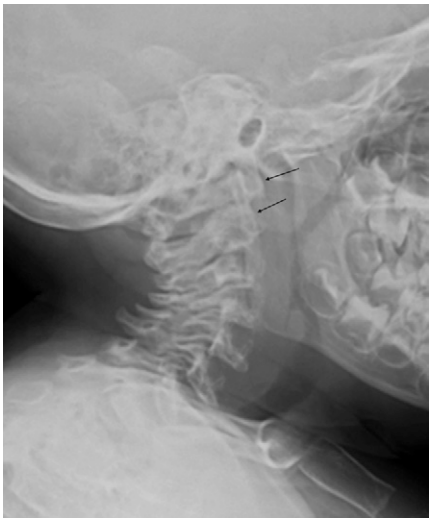


Fig. 1-A

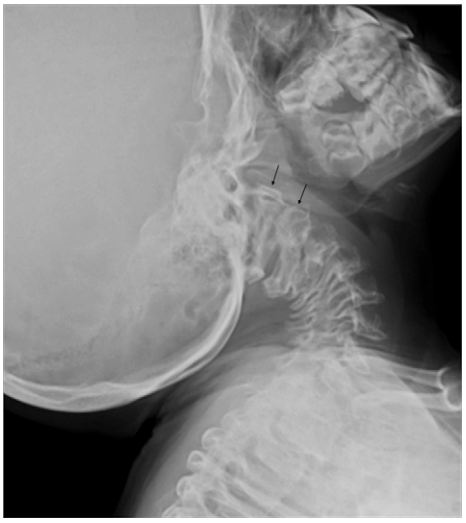


Fig. 1-B

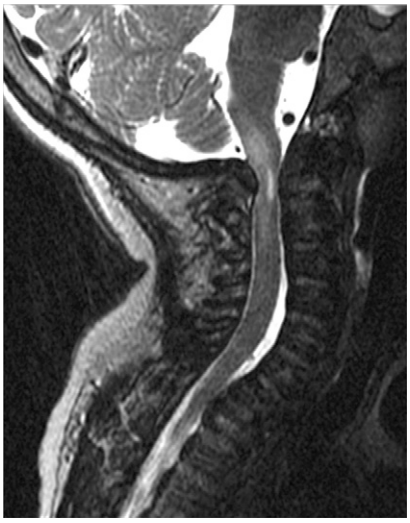


Fig. 1-C

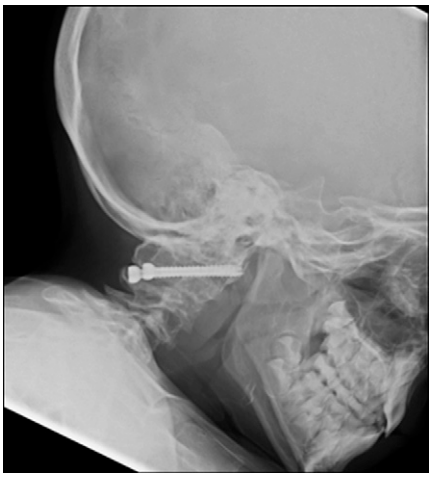


Fig. 1-D

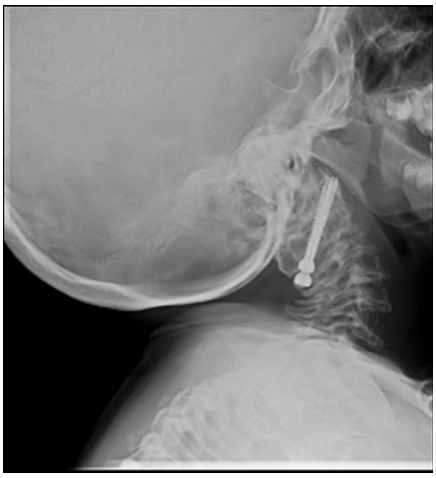


Fig. 1-E

Radiographs and MRI showing a patient with Morquio syndrome who underwent C1-C2 fusion. This patient had limited flexion; however, notable instability is present in the views between flexion (**Fig. 1-A**) and extension (**Fig. 1-B**). Anterior borders of C1 and C2 are depicted with arrows. Cord compression and signals changes were visible on the T2 MRI sagittal view. There is notable posterior compression by the posterior arch of C1 (**Fig. 1-C**). C1-C2 stability was achieved with transarticular screws. Lateral radiographs made with the cervical spine in flexion (**Fig. 1-D**) and extension (**Fig. 1-E**) show a stable fusion mass at three years postoperatively.

Preoperative Imaging Findings

We reported the preoperative imaging of ten patients (Table I). The mean space available for the cord was 13.3 mm in extension and 10 mm in flexion. Of these ten patients, nine had preoperative MRI and some degree of cord compression and five had signal changes in the cord. The mean anteroposterior diameter of the dura was 7 mm, which was measured between the odontoid and the posterior arch of the atlas. The MRI and lateral spine radiographs showed that five of the ten patients also had kyphotic deformity at the cervicothoracic junction without apparent cord compression, and six of the ten patients had kyphotic deformity at the thoracolumbar junction.

Implant

Five patients had posterior in situ fusion without use of any implant; postoperative stabilization was achieved with a halo vest or halo cast. The only pseudarthrosis was in this group of patients. For internal fixation, cables were used in six patients and wires were used in six patients (see Appendix). In three patients, transarticular screws were used with or without cable augmentation. Figure 1 shows a patient managed by means of transarticular screw fixation. The decision to use transarticular screws was made after examining the preoperative CT scans.

Graft

Of the eight patients who underwent index cervical fusion at our institution, autograft was harvested from the iliac wing in seven patients and from the autologous rib in one patient. We were not able to retrieve the bone graft records for the twelve patients who underwent index cervical fusion elsewhere.

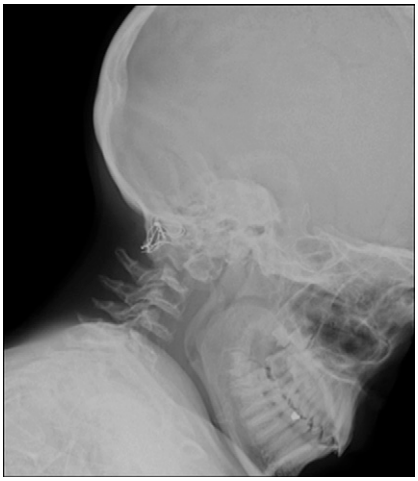
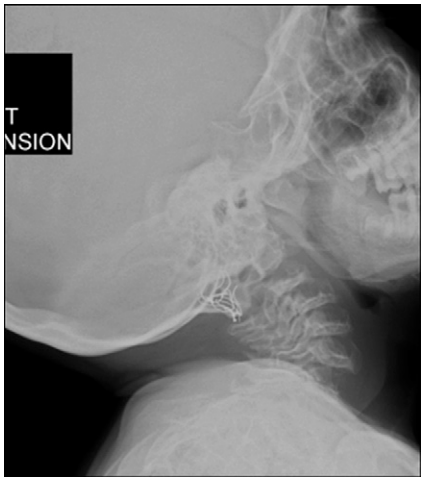


Fig. 2-A



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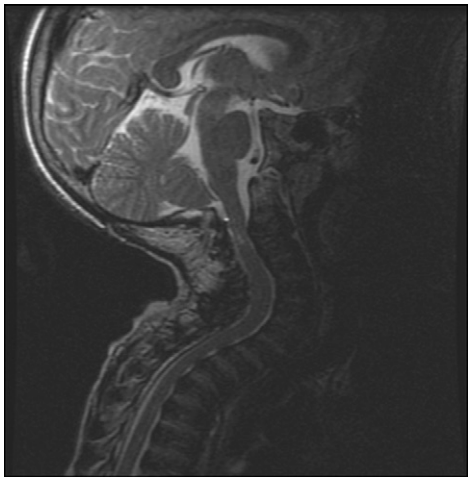

Fig. 2-C

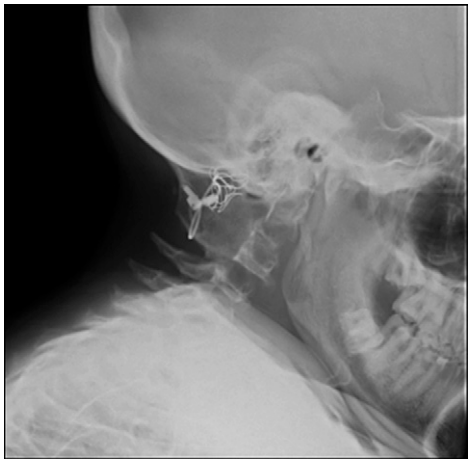

Fig. 2-D

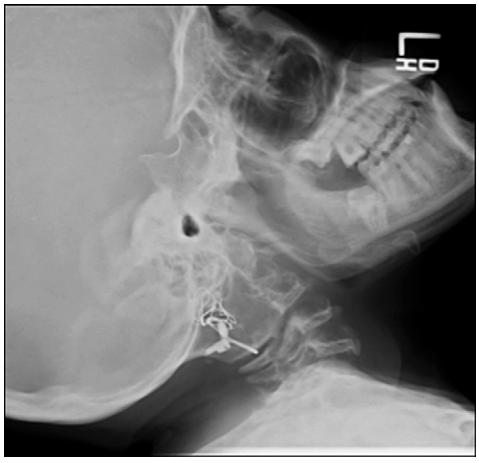

Fig. 2-E

Radiographs and MRI showing a patient who had previously undergone occiput-C2 fusion with autograft and wire stabilization. Instability between the fusion mass and C3 was visible on lateral radiographs made with the cervical spine in flexion (**Fig. 2-A**) and extension (**Fig. 2-B**). The MRI sagittal view also demonstrated compression of the cervical cord with intrinsic signal changes on T2 sequences (**Fig. 2-C**). The patient underwent extension of the fusion to C4 with autograft and fixation with cables. Lateral radiographs made with the cervical spine in flexion (**Fig. 2-D**) and extension (**Fig. 2-E**) show a stable fusion mass at five years postoperatively.

Immobilization Type and Period

Nine patients were externally immobilized with use of either a halo cast or a halo vest for six to twelve weeks depending on where the surgery was done and the time period. One patient was immobilized with use of a Minerva jacket, and no internal fixation was used in this patient. One patient with transarticular screw fixation used a cervicothoracic orthosis for three months. For the remaining nine patients, we were not able to retrieve the immobilization records.

Revisions

Seven patients required an extension of fusion to a lower level. Six patients required a caudal extension of fusion to C3-C5 levels (Table II). The mean interval between the initial surgery and the revision surgery was ninety-five months (range, thirty-six to 168 months). The indication for revision surgery for these six patients was instability at the distal level with or without MRI signal changes in the cervical spinal cord. The fusion level was extended to C3 in one case, C4 in three cases, and to C5 in two cases. In the remaining patient, fusion was extended to T2 because of distal junctional instability and multilevel stenosis with cervicothoracic kyphosis about twenty months after the initial surgery. Figure 2 shows a patient who had undergone treatment for symptomatic instability. The average time to follow-up after the revision fusion was fifty-two months (range, six to 114 months).

The only patient with symptomatic pseudarthrosis (patient number 12, Table II) underwent C1-C2 transarticular screw fixation. The original occiput-C2 fusion of this patient was done at an outside facility without use of internal fixation.

Two patients required decompression and fusion of levels unrelated to upper cervical instability. One patient whose fusion was extended to T2 had to be fused to T7 twelve years after his last fusion extension to T2. At that time, he had progressive neurologic decline secondary to thoracic-level stenosis. One other

TABLE II Revision Surgeries Secondary to Distal Junctional Instability and Cord Compression

Patient No.	Revision	Time to Revision* *(mo)*	Indication
1	C2-C4	36	Instability
5	C2-C3	72	Instability
7	C2-C4	125	Instability and myelomalacia
10	C2-T2	168	Neural symptoms and myelomalacia
12	C1-C2	124	Pseudarthrosis
13	C2-C4	108	Instability
19	C2-C5	48	Instability
20	C2-C5	77	Neural symptoms

*The mean time to revision was 94.8 months.

patient displayed stenosis at C7-T1 and had decompression of these levels along with fusion between C7 and T4 during her upper cervical fusion. All patients were neurologically and mechanically stable at the time of the latest follow-up.

Neural Outcome

One patient was not walking at the time of the latest clinic follow-up and had not been walking preoperatively. Six patients were independent walkers who did not use any assistive device. The remaining thirteen patients independently walked at home but required a walker or a scooter in the community. Except for one patient, whose walking status improved after surgery, overall neural status and neurologic examination were minimally changed. None of the patients' neural statuses deteriorated after the fusion procedure.

Discussion

The mucopolysaccharidoses are a group of metabolic disorders, each characterized with a lysosomal enzyme defect. These disorders result in an accumulation of different types of mucopolysaccharides in the cell, leading to central nervous, cardiovascular, pulmonary, ophthalmologic, auditory, and musculoskeletal disorders. Mucopolysaccharidosis type IV (Morquio syndrome) has predominantly orthopaedic manifestations with severe spinal problems.

Morquio syndrome was first described by Morquio[13,14] and Brailsford[15] in 1929. This rare autosomal-recessive genetic disorder is characterized by the absence of or reduction in the activity of the N-acetylgalactosamine-6-sulfate sulfatase (GALNS) enzyme for Morquio type A[16] or the B-galactosidase enzyme for Morquio type B[17]. These enzyme deficiencies lead to a lack of degradation of keratan sulfate and cause clinical features of skeletal dysplasia through excessive intracellular accumulation. The diagnosis is established by physical and radiographic features, deficiency of the related enzyme activity in cultured fibroblasts, excessive keratan sulfate in urine, and confirmation by the GALNS enzyme assay[5,6]. Prenatal diagnosis is also possible through electrophoresis of the amniotic fluid glycosaminoglycans[18].

Patients with Morquio syndrome appear healthy at birth, as do other patients with mucopolysaccharidosis[19]. Disease-specific radiographic changes have been observed prior to clinical signs and symptoms, which present usually by the third year of life. Typical features are disproportionate (short trunk) dwarfism, pectus carinatum, kyphosis, scoliosis, genu valgum, flaring of the lower ribs, hypermobile joints, and an abnormal and unstable gait[5]. Children with Morquio syndrome have odontoid hypoplasia, ligamentous laxity, and extradural mucopolysaccharide deposition, adding to the spinal cord compression[2,4,5]. Early cervical spine management with prophylactic fusion has been recommended to prevent cervical myelopathy[1,6]. Prophylactic fusion was reported to have better neurologic outcomes compared with fusions done after neural compromise[1,6]. It has also been documented that, in patients with upper cervical instability, cervical fusion prevents the otherwise progressive neurologic compromise[2,20-30].

With use of CT myelography, Stevens et al.[2] studied the upper cervical spine of thirteen patients with Morquio syndrome. They described the pathoanatomy of the upper cervical spine in detail and reported that atlantoaxial instability was mild and subluxation was absent in the majority of their cases. They reported that the severity of neurologic involvement was related to the anterior extradural soft tissue. This finding is consistent with the MRI findings by Hughes et al.[4] and implies that direct radiography underestimated the amount of cord compression in patients with Morquio syndrome. Ransford et al.[6] reported the results of upper cervical fusion in seventeen patients with Morquio syndrome, including the thirteen from the study by Stevens et al. Ransford et al. emphasized that the os odontoideum or cartilaginous dens were an indicator of C1-C2 instability and ossified once fusion was accomplished and stability was achieved. They also reported that demonstrable instability on lateral radiographs of the cervical spine in flexion and extension was a late feature and almost invariably was associated with myelopathic findings. Therefore, they recommended prophylactic fusion to prevent instability and myelopathic signs. However, the follow-up period for this study was not shown.

Morquio syndrome is a rare disease; hence, many upper cervical fusion reports are on groups of patients with heterogeneous diagnoses and short to intermediate-term follow-up[20,23,30,31]. Ain et al.[20] reported their experience of upper cervical fusion in a variety of skeletal dysplasias, including seven patients with Morquio syndrome. They achieved osseous union with use of iliac crest autograft in all patients with Morquio syndrome. They did not provide information on internal fixation. Six of these patients had neurologic compromise preoperatively, and five of them improved after surgery. Ain et al. did not observe any instability distal to the fused levels in their patients; however, their mean follow-up period was 5.1 years, with three of the seven patients having a follow-up of less than three years.

Pouliquen et al.[31] reported the results of cervical instability treatment in six patients with Morquio syndrome with a follow-up of one year. They reported nonunion and neurologic compromise in one of their patients. Both Koop et al.[23] and Svensson and Aaro[30] reported the results of upper cervical fusion in patients with skeletal dysplasia, with only one patient with Morquio syndrome in each study. They reported solid fusion in both of these patients. In a review paper on Morquio syndrome, Northover et al.[7] noted abnormal motion occurring below successfully fused segments.

The current study shows intermediate to long-term follow-up results of upper cervical fusion in twenty patients with Morquio syndrome. The rarity of this metabolic disorder precludes a large series, yet, to our knowledge, this study shows the largest number of patients with Morquio syndrome who underwent upper cervical fusion with a mean follow-up period of almost nine years. Our imaging findings show that the actual space available for the cord is largely underestimated with direct radiology because of the unossified odontoid tip and soft-tissue deposition posterior to the odontoid, anterior to the spinal cord. These findings are in concordance with previous reports and underline the importance of surveillance of cervical instability in patients with Morquio syndrome. Currently, in children with suspected spinal cord compression, neural changes, and instability, we utilize flexion-extension cervical spine MRI under general anesthesia or sedation. The safety and utility of flexion-extension MRI in patients with skeletal dysplasia have been recently shown[32], and our indications to acquire a flexion-extension cervical spine MRI study are in line with this report.

The data from the current report show that fusion can be reliably expected after posterior upper cervical fusion with use of an internal fixation method and autograft. However, distal junctional instability requiring additional surgery was observed in 40% of our patients.

Upper cervical instability in Morquio syndrome can reliably be addressed with occiput-C2 fusion, and a stable neurologic outcome can be expected. However, long-term follow-up of these patients is mandatory, as distal junctional instability and spinal cord compression may develop in a large portion of these patients. We believe that upper cervical fusion is indicated in the absence of clinical symptoms if radiographic signs of progressive instability and/or cord compression are present, given the drastic complications of spinal cord compression and the better neurologic outcome. Patients and families should be informed about this frequent complication and the probable need for secondary surgical interventions requiring extension of fusion to lower levels. Whole spine imaging is required to screen for cord compression at the cervicothoracic and thoracolumbar junctions in addition to the craniocervical junction.

Appendix

eA A table showing the patient demographic characteristics, fusion levels, and internal fixation methods is available with the online version of this article as a data supplement at jbjs.org. ■

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