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The Management of Kyphosis in Metatropic Dysplasia

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Abstract

Design: Retrospective review.
Objective: To describe the presentation and progression, and compare treatments of severe thoracic kyphosis in a cohort of patients with metatropic dysplasia.
Summary of Background Data: Metatropic dysplasia is a rare skeletal dysplasia characterized by several abnormalities, including severe platyspondyly and vertebral wedging. These lead to marked kyphoscoliosis that begins in the first year of life and progresses to a stiff, short thorax and restrictive lung disease. There is no study that specifically addresses treatment of kyphosis in this cohort.
Methods: A 12-year retrospective chart review at a single institution was performed to identify metatropic dysplasia patients. Comparison between four main treatment groups—observation, bracing, anterior release and growing construct, and anterior release and final fusion—were made radiographically with regard to thoracolumbar, T2–T12, and major Cobb kyphosis; sagittal vertical alignment; and C7–kyphosis apex distance, taken at presentation, pre- and posttreatment, and final follow-up.
Results: Twenty patients with metatropic dysplasia presented at an average age of 3.1 years with a kyphosis of 75°, and were followed an average of 8.5 years. Those treated surgically presented with an average of 86.7° kyphosis, 88 mm C7–kyphosis apex distance, and 50 mm positive sagittal vertical alignment (SVA). Postsurgical reduction of kyphosis averaged 43° with less than 4° loss of correction in all groups except the constructs involving rib fixation. Recent use of staged thoracoscopic anterior soft tissue release, halo traction, and growing rod construct has produced the most dramatic results with average kyphosis correction of 71° and evidence of anterior bony remodeling. In those treated with observation, kyphosis progressed less than a quarter degree per year.
Conclusions: Thoracic kyphosis in metatropic dysplasia does not uniformly progress in all patients and therefore can be initially observed. In those who progress, several surgical options exist including growth-friendly constructs that have demonstrated success without a higher rate of complications.
Level of Evidence: Level IV.

Keywords: Metatropic dysplasia; Kyphoscoliosis; Kyphosis; Skeletal dysplasia; Skeletal dysplasia spine

Introduction

Metatropic dysplasia is a rare skeletal dysplasia characterized by a short-limbed, short-trunk dysplasia with articular abnormalities and kyphoscoliosis. Originally described by Maroteaux et al. in 1966 [1], the rhizomelic dysplasia was named for its characteristic change to short-trunk dwarfism as kyphoscoliosis progresses, thus "metatropic" from the Greek "meta-" and "tropos" meaning "to change pattern." The syndrome was originally thought to be part of a genetic spectrum [2,3], but recent genetic discoveries have mapped the disorder to a de novo autosomal dominant activating mutation of the transient receptor potential cation channel, subfamily V, member 4 gene (TRPV4) [4]. Variation of mutations within the gene may account for the range in presentation severity [2,3,5-7]. In the spine, the altered growth causes several vertebral abnormalities, including severe platyspondyly and vertebral wedging, which lead to marked kyphosis that begins in the

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first year of life and progresses to a stiff, short thorax and restrictive lung disease [7-12]. Spinal stenosis with a natural history of myelopathy results from the progressive deformity.

Despite its namesake deformity, kyphosis treatment in metatropic dysplasia has had limited attention in the literature, owing to the rare incidence of the syndrome, with few prior studies discussing natural history. The purpose of this study is to describe the presentation, progression, and modern treatment of severe kyphosis in a large cohort of patients with metatropic dysplasia treated at a single institution.

Materials and Methods

With institutional review board approval, we performed a retrospective review of more than 18,000 continuous visits to our skeletal dysplasia clinic from 2004 to 2016 and identified 24 individuals with a diagnosis of metatropic dysplasia. These charts were examined for basic demographics, age at presentation and diagnosis, spine symptoms, kyphosis treatment and indications, and treatment follow-up, including perioperative complications or conservative treatment failure. Upright radiographs were reviewed and measured with regard to thoracolumbar (T11−L2), T2−T12, and major Cobb kyphosis; sagittal vertical alignment (SVA); and C7−kyphosis apex distance, each taken at initial presentation, pre- and posttreatment, and final follow-up, as applied to each individual (Fig. 1). Major Cobb kyphosis, which is the measurement that captures the entire kyphotic curve, was used rather than thoracic T2−T12 kyphosis because this patient population's kyphosis apex falls in the thoracolumbar region; thus, the most distal portion of the kyphosis was often distal to T12. Exclusion criteria included any patient found to have a diagnosis other than metatropic dysplasia, or for whom at least two separate radiographic timepoints at least one year apart did not exist.

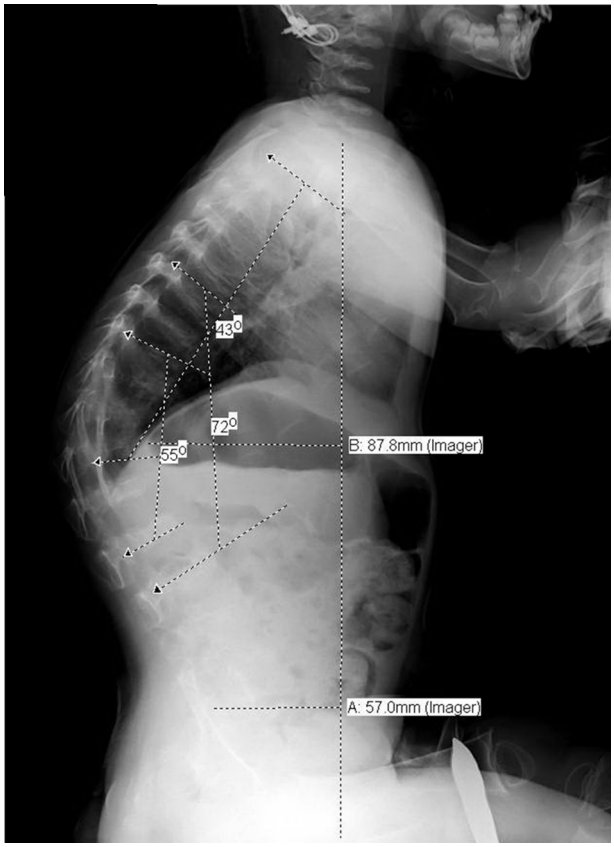

Fig. 1. Radiographic measurements. Thoracic kyphosis, measured from T2−T12 = 43°. Major Cobb kyphosis, measured from most tilted vertebra = 72°. Thoracolumbar kyphosis, measured from T11−L2 = 55°. A: 57 mm = sagittal vertical alignment (SVA). B: 88 mm = C7−kyphosis apex distance.

Results

There were 20 metatropic dysplasia patients with at least two different erect lateral spine radiographs to compare, consisting of 16 males (80%) and 4 females (20%). The average age at presentation to our clinic was 3 years 1 month, and the average age at first erect radiograph was 4 years. The average initial presenting thoracolumbar kyphosis was 48°; the average initial presenting thoracic (T2−T12) kyphosis was 53°; and the average major Cobb kyphosis was 75°. Three patients had initial radiographs without a standard measurement magnification for accurate distance measurement; for the other 17, the average presenting SVA was 34 mm (range −17 to 112 mm; median 91 mm) and C7−kyphosis apex distance was 100 mm (range 19−116 mm; median 93 mm). Patients were followed an average of 8.4 years (range 1.5−20.6 years; median 7.75 years), and average age at last documented spine radiograph was 11.5 years.

Four main treatment strategies were employed: observation; thoracolumbosacral orthosis (TLSO); staged anterior release with two to four weeks halo traction and posterior growing construct (four expandable spine/pelvis-to-rib constructs, two spine-to-spine magnetically controlled growing rod constructs [MCGR]); and staged anterior release and definitive posterior fusion. Table 1 compares the average patient characteristics and radiographic parameters between the different treatments. The group sizes preclude meaningful statistical analysis, but comparing medical/interventional versus operative patients, the surgical patients presented, on average, with 30° more thoracolumbar kyphosis, 12° more thoracic kyphosis, 19° greater Cobb kyphosis, 50 mm greater C7 to kyphosis apex distance, and 29 mm greater SVA. Indication for operative intervention was demonstrated progressive kyphosis beyond at least 95° or cord compression at the kyphosis as seen on magnetic resonance imaging (MRI) or through clinical symptoms. Fourteen patients had MRIs done preoperatively in our system, 10 with evidence of cord compression, and 17 had high cervical fusion and/or

Table 1
Average presenting demographic and radiographic characteristics grouped by eventual treatment type.

Treatment type	Patients (n)	Age (years)	Average follow-up (years)	Thoracolumbar kyphosis (T10–L2, degrees)	Thoracic kyphosis (T2–T12, degrees)	Cobb kyphosis (degrees)	C7–kyphosis apex distance (mm)	Sagittal vertical alignment (mm)
Observation	8	3.4 (0.4–13.3)	6.1 (1.2–10.7)	39.6 (15–70)	51.1 (28–84)	69.1 (42–115)	40.2 (18–70)	23.0 (−17 to 57)
TLSO brace	5	2.3 (0.7–6.0)	8.1 (3.8–14.0)	33.0 (10–53)	45.8 (28–78)	66.8 (53–90)	38.6 (22–47)	25 (8–42)
Anterior release + spine-to-rib growing rods	4	3.6 (0.3–6.0)	4.9 (2.1–7.7)	69.8 (49–83)	67.3 (30–93)	90.3 (75–111)	81.6 (72–100)	32.4 (4–81)
Anterior release + final fusion	1	14.8	4.1	54.0	46.0	83.0	116	113
anterior release + spine-to-spine MCGR	2	2.8 (1.3–4.3)	3.8 (1.7–5.8)	67.0 (55–79)	56.5 (43–70)	81.5 (72–91)	88.5 (88–89)	53.3 (50–57)

MCGR, magnetically controlled growing rod; TLSO, thoracolumbosacral orthosis.
Presenting age was reported as the first visit to clinic; presenting radiographs were reported as the first obtained erect sagittal spine radiograph.

decompression for cervical instability before treatment of their kyphosis. One patient was surgically treated at 83° because of coronal plane scoliosis of 90° and failed attempt at brace wear, and another at 88° due to severe apical spinal stenosis on MRI and lower extremity radiating pain. Two patients with Cobb kyphosis of 101° and 115° had no progression and thus were treated with observation. These patients demonstrate that because of the vertebral wedging and platyspondyly, the kyphosis is sometimes a fixed structural deformity that does not progress or cause neurologic symptoms and therefore is not indicated for surgery. Two patients with expandable spine/pelvis-to-rib constructs were later converted: one to an MCGR to avoid frequent return to surgery, the other to a dual pelvis-to-rib construct for painful prominent implant. The latter patient then went on to final fusion.

The average change in radiographic measurement for each treatment type is shown in Table 2, and the major Cobb kyphosis measurements for all groups across each recorded time point is illustrated in Figure 2. A clinical example is shown in Figure 3. Kyphosis progression in patients treated with observation was less than a quarter of a degree gained per year for all kyphosis measurements, and a +3 mm change in SVA per year, that is, a worsened

Table 2
Average change in kyphosis after surgical treatment.

Treatment type	Thoracolumbar kyphosis (T10–L2, degrees) change	Thoracic kyphosis (T2–T12, degrees) change	Cobb kyphosis (degrees) change	C7–kyphosis apex distance (mm) change	Sagittal vertical alignment (mm) change
Anterior release + spine/pelvis-to-rib growing rods	−47.3 (−73 to −26)	−24.5 (−53 to −12)	−32.5 (−41 to −24)	−50.5 (−55 to −47)	−30.2 (−59 to 8)
Anterior release + final fusion	−19.0	−10.0	−31.0	−64.2	113
Anterior release + spine-to-spine MCGR *Conversions/complete revision	−49.5 (−52 to −47)	−65.5 (−75 to −56)	−70.5 (−71 to −70)	−70.8 (−85 to −57)	−20.5 (−28 to −13)
Anterior release + spine-to-rib → MCGR	−26	−45	−44	−28	4.9
Anterior release + spine/pelvis-to-rib → Dual pelvis-to-rib	−7	−1	−13	−12.3	−11.4
Pelvis-to-rib → final fusion	0	−8	−26	−9.6	−22.5

MCGR, magnetically controlled growing rod; TLSO, thoracolumbosacral orthosis.
The change between immediate preoperative and postoperative erect radiographic measurements compared between surgical treatments, reported as group average and range. Negative number denotes loss of kyphosis or decreased sagittal alignment distance, and positive denotes gain of kyphosis or increased sagittal alignment distance.
* Two patients were converted: one patient had a single conversion to an MCGR (first conversion row); one patient had a conversion from single spine/pelvis-to-rib growth construct to a dual pelvis-to-rib growth construct, and then another conversion to final fusion (second and third conversion rows, outlined together).

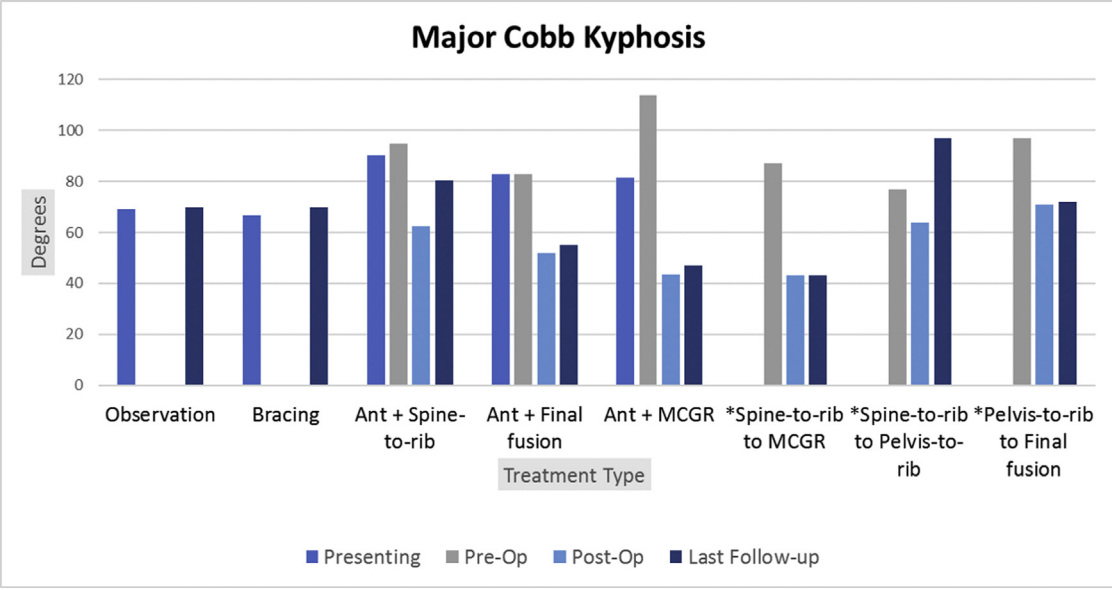

Fig. 2. Major Cobb kyphosis within treatment groups across measured timepoints. *Single patient conversions, where ''Last Follow-up'' is either the last follow-up or the last measurement before the next conversion surgery. Note that kyphosis at last follow-up for those with rib fixation (Spine-to-rib to Pelvis-to-rib) shows worse kyphosis as compared with preoperative kyphosis; these represent the same preoperative cohort for pelvis-to-rib conversion to final fusion.

sagittal alignment. The bracing cohort had a 0.02° kyphosis increase per year, and a −1 mm change in SVA, which is in the direction of improved sagittal alignment. Postoperative kyphosis correction was largest in the MCGR group (70.8° on average), with similar correction achieved in final fusion and rib-fixation growing construct groups.

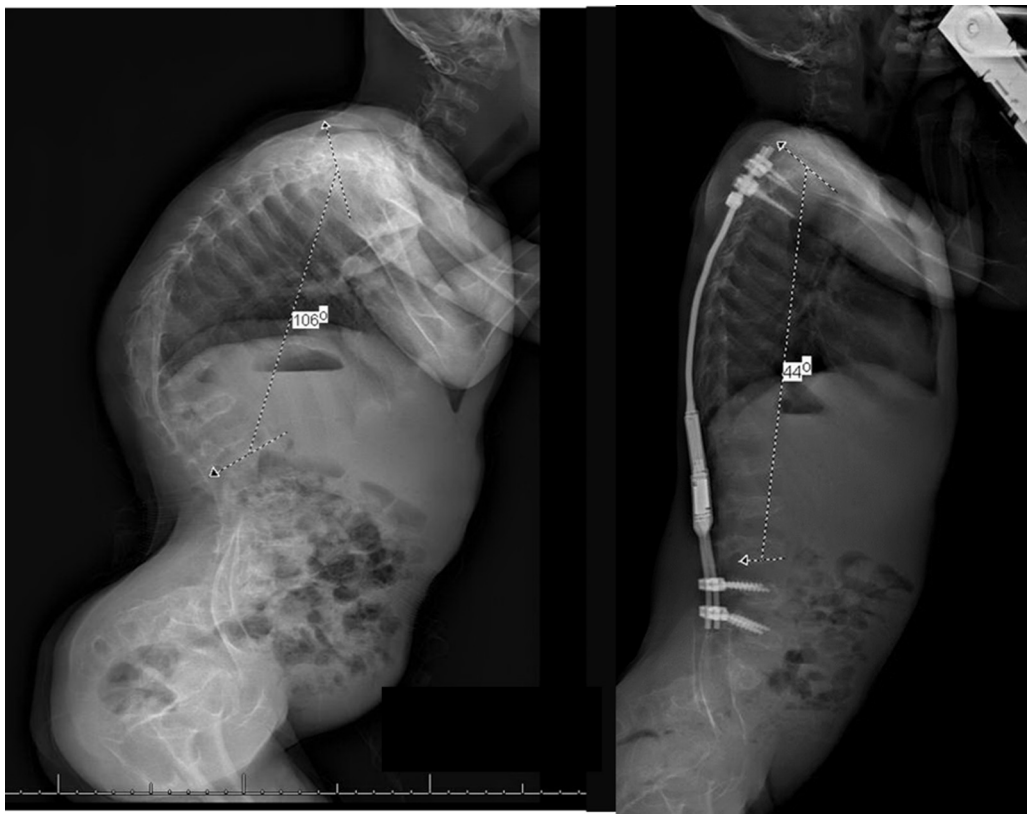

Fig. 3. Clinical example. This patient had progressive kyphosis and was treated with an anterior release and growing construct. Major Cobb kyphosis improved from 106° to 44°.

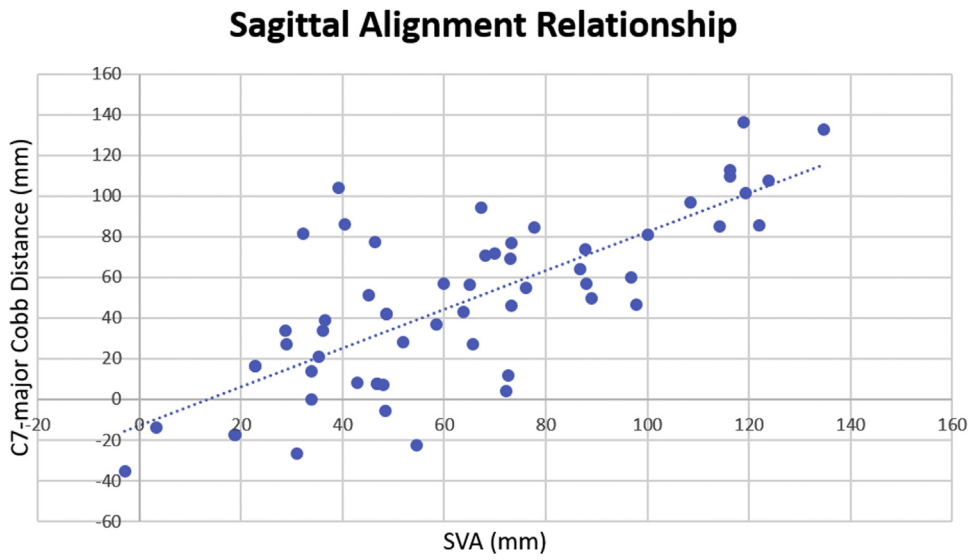

Fig. 4. Sagittal alignment relationship. C7 major Cobb distance versus sagittal vertical alignment (SVA). Linear relationship is the best-fit average line of the value points.

Coronal plane scoliosis was seen in 14 patients at their initial radiograph and averaged 45°. At final follow-up, the average coronal Cobb was 22°. Three of the six patients who did not originally present with scoliosis did develop scoliosis at the final follow-up of an average of 26°.

Initial presenting sagittal balance by SVA was positive in all patients except for three that were managed by observation. SVA to C7 plumb line distance had a strong linear correlation (Fig. 4) for all radiographs both pre- and post-treatment. Major kyphosis Cobb angle correlated less strongly with each of these two sagittal measurements (Fig. 5): in other words, achieving improved kyphosis Cobb angle through treatment did not cause an equal improvement in sagittal balance.

All complications in the cohort occurred in the spine/pelvis-to-rib growing constructs. There were two neuromonitoring changes that did not resolve intraoperatively. One occurred during a spine-to-rib conversion to final fusion. The case was aborted, full motor function returned, and the fusion was completed ten days later without any long-term effects. The other occurred during an initial spine/pelvis-to-rib instrumentation. Although the motor and

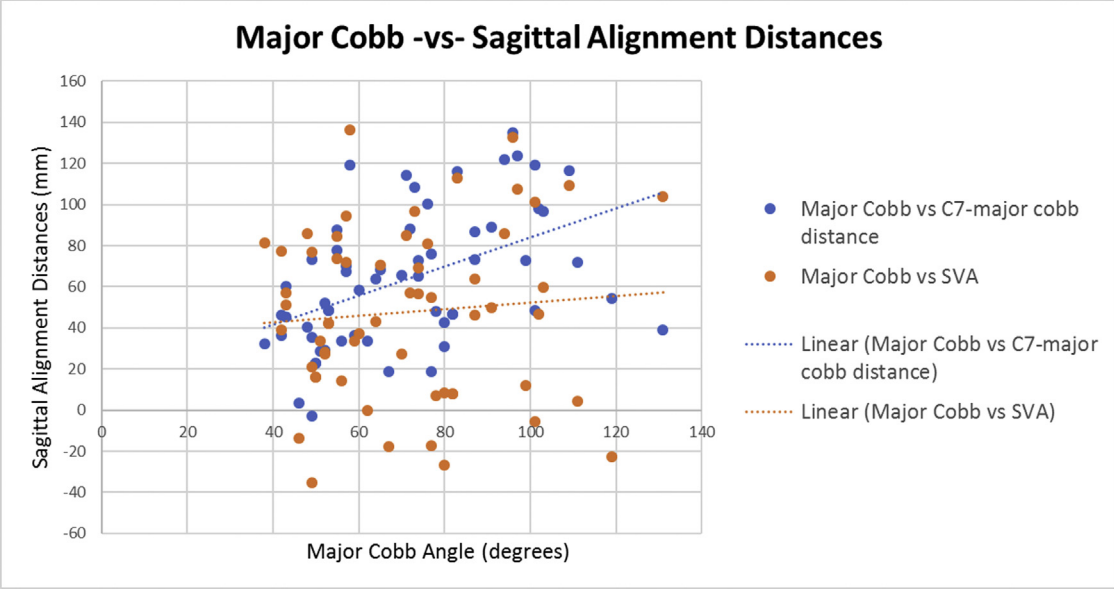

Fig. 5. Relationship of major Cobb kyphosis versus sagittal alignment balance, as measured by SVA and C7–major Cobb distance. Linear relationship is the best-fit average line of the value points.

sensory neuromonitoring changes appeared to resolve intraoperatively and the patient was ambulating immediately after surgery with 5/5 strength, permanent conus injury remained with bowel and bladder function deficits. This same patient later had painful prominent hardware that led to conversion to a dual pelvis-to-rib construct. This construct then experienced a number of separate complications requiring revision during surgical lengthenings including a broken rod, four episodes of loss of rib fixation, and one loss of pelvic fixation. One other patient had loss of rib fixation with revision rib fixation performed at the next planned surgical lengthening.

Discussion

This is the first case series to look specifically at kyphoscoliosis treatment in metatropic dysplasia, and to our knowledge is the largest review of patients with this rare disease. The largest prior study was a cohort of 19, which did not include a description of their treatment or natural history [13]. Kannu et al. reported on a historical, long-term cohort of seven patients who lived past infancy, and three were fused for kyphosis [9]. Another study used these seven patients and included eight more to compare attributes across a TRPV4 mutation spectrum, including whether kyphoscoliosis was present or not, but did not discuss measurements, treatment, or natural history [14]. Others have reported on the typical cervical spine anomalies of metatropic dysplasia including odontoid hypoplasia, instability, stenosis, and their treatments [15,16], and these found up to a 44% rate of surgical complications.

Single or small case studies have described a range of kyphosis treatment in MD with assorted complications, including a single rod with hook distraction that cut out [17], decompression without fusion lacking symptom improvement [18], and posterior fusions with pseudarthrosis [9,18]. Successful preoperative halo-gravity traction and subsequent posterior spinal fusion for kyphoscoliosis has been previously described in a small cohort of dysplasias, and did include two patients from this MD group [19]. In other skeletal dysplasias, use of traditional and rib-based growing constructs have shown a 50% rate of revision [20]. In our cohort, rib-based growing constructs accounted for all our complications and may not be a suitable strategy in this population. There were no complications from MCGR over an average postoperative follow-up time of 3.75 years in this group, nor pseudarthrosis in patients with final fusion at an average of 2.5 years' postoperative follow-up. These patients fared better than the historical cohorts noted above.

The efficacy of bracing cannot be determined from our cohort, as bracing results did not significantly differ from observation alone. Although we do not know if these patients would have otherwise progressed, their average pre-brace kyphosis was less than the average observed kyphosis; thus one might assume that they would not have. Moreover, compliance with and duration of brace wear was not reliably recorded.

Limitations of this study are related to the retrospective study design and small sample size. There was no uniform protocol for treatment, either in indication for treatment or type of treatment. However, in general patients were indicated for treatment with neurologic symptoms, a pattern of radiographic progression, or evidence of cord compression at the kyphosis apex on MRI. We did not have a large enough cohort to make statistical comparisons between the treatment types, but the surgical choices in most cases represented the technology available at the time and the skeletal maturity of the patient. Follow-up until the patients reached their adult height would strengthen further studies for a more longitudinal understanding of the natural and posttreatment history of kyphosis in these patients. This longer follow-up would be particularly important given the continued positive sagittal alignment in many patients at our final follow-up, and the possibility that this could lead to later decompensation.

Another weakness is that measurements were performed by a single practitioner, but because these were not statistically compared against one another, inter- and intrarater reliability would not have affected the overall findings of the paper. We also did not have a standardized standing position for the lateral radiographs across the course of this study, which can affect the SVA based on upper extremity positioning. All were taken standing upright, however, unless the child was too young to stand, in which case seated upright position was used. Because standard kyphosis measurements of the thoracic (T2–T12) or thoracolumbar (T10–L2) spine did not capture each patient's global kyphosis because of varying levels of the apex, major Cobb kyphosis was primarily used in the discussion of results, but all were reported in the tables. This major Cobb measurement has been demonstrated to have an intraobserver reliability of 4° [21] and interobserver reliability of 7° to 13° [22,23].

This is the first study to examine kyphosis in the unique and rare population of metatropic dysplasia patients. Our treatment algorithm is to monitor patients with upright radiographs. Any neurologic symptoms or pain preventing daily activities indicates an MRI. Findings of cord compression lead to surgical intervention, as does demonstrated progression upward of 90°. In this group of patients, a major kyphosis greater than 95° commonly, but not universally, progressed and was therefore treated surgically. Patients nearing skeletal maturity underwent final fusion, whereas those still immature underwent a growth-friendly technique. A staged anterior release and halo traction followed by posterior spinal fusion or spine-based growing construct has been successful at correcting and maintaining kyphosis correction with less complications than previously reported. Long-term follow-up into adulthood is needed to determine if residual positive sagittal balance leads to later decompensation.

Key points

- Thoracolumbar kyphosis in metatropic dysplasia is not uniformly progressive, but commonly severe in early childhood.
- Staged anterior soft tissue release, halo traction, and growing rod construct produced the best results for kyphosis correction and allowed further thoracic growth.
- Rib-based constructs resulted in a higher rate of complications.

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