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Minireview

Diagnostic evaluation, monitoring, and perioperative management of spinal cord compression in patients with Morquio syndrome

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ABSTRACT

Mucopolysaccharidosis IVA is an autosomal recessive condition caused by mutations in the *GALNS* gene, which encodes N-acetylgalactosamine-6-sulfatase, also called galactosamine-6-sulfatase (GALNS). A reduction in or absence of effective GALNS leads to faulty catabolism of keratan sulfate and chondroitin-6-sulfate within the lysosome; their accumulation causes cell, tissue, and organ dysfunction. The connective tissue, cartilage, ligaments, and bone of patients with Morquio A syndrome are particularly affected. Patients with Morquio A syndrome are at high risk of neurological complications because of their skeletal abnormalities; many patients are in danger of cervical myelopathy due to odontoid hypoplasia and ligamentous laxity leading to atlantoaxial subluxation. The multisystemic involvement of patients with Morquio A syndrome requires treatment by multidisciplinary teams; not all members of these teams may be aware of the potential for subluxation and quadriparesis. A multinational, multidisciplinary panel of 10 skeletal dysplasia or Morquio A syndrome specialists convened in Miami, FL on December 7 and 8, 2012 to develop consensus recommendations for early identification and effective management of spinal cord compression, for anesthesia and surgical best practices, and for effectual cardiac and respiratory management in patients with Morquio A syndrome. The target audience for these recommendations includes any physician who may encounter a patient with Morquio A syndrome, however doctors who do not have access to the full spectrum of specialists and resources needed to support patients with Morquio A syndrome should attempt to refer patients to a center that does. Physicians who manage Morquio A syndrome or comorbid conditions within specialty centers should review these expert panel recommendations and fully understand the implications of spinal cord instability for their own practices.

Contents

Abbreviations: C6S, chondroitin-6-sulfate; ERT, enzyme replacement therapy; GAGs, glycosaminoglycans; *GALNS*, the gene encoding N-acetylgalactosamine-6-sulfatase; GALNS, the protein N-acetylgalactosamine-6-sulfatase, also known as galactosamine-6-sulfate sulfatase; KS, keratan sulfate; MEP, motor evoked potentials; SSEP, somatosensory evoked potentials.

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1. Introduction

Mucopolysaccharidosis IVA (OMIM #253000; eponyms Morquio A, Morquio–Brailsford) is an autosomal recessive condition caused by mutations in the gene encoding N-acetylgalactosamine-6-sulfatase, also known as galactosamine-6-sulfate sulfatase (OMIM #612222) (EC 3.1.6.4) [1–3]. GALNS catabolizes the GAGs KS and C6S [4,5]. A reduction or absence of GALNS activity leads accumulation of KS and C6S and within the lysosome, resulting in cell, tissue, and organ dysfunction. The connective tissue, cartilage, ligaments, and bone of patients with Morquio A syndrome are particularly affected [6,7].

Patients with Morquio A syndrome may appear normal at birth, but bony deformities of the knee, spine, or chest, can appear during the first year of life, although diagnosis may not be made until later [8,9]. The brain and spinal cord are not directly affected by GAG accumulation, and intelligence is preserved, although opportunities for education may be curtailed by physical limitations [10–12]. Many patients are at risk for developing cervical myelopathy due to atlantoaxial subluxation from odontoid hypoplasia and ligamentous laxity. Cervical myelopathy is common in the more severe forms of the disease [13,14].

Although the hallmarks of Morquio A syndrome are skeletal, multiple other systems may be compromised: visual, auditory, digestive, cardiovascular, neurological and respiratory [15]. A variety of surgical procedures may be undertaken in patients with Morquio A syndrome, including decompression/cervical fusion or other spine surgery, myringotomy, hip surgery, osteotomies (especially at the knee), tonsillectomy, adenoidectomy, and herniorrhaphy, and most patients will require multiple procedures [16] by the age of 12 years [8]. A survey of 325 patients with Morquio A syndrome found that more than 70% of patients older than 5 years required some type of surgery [16]. A wide array of specialists care for patients with Morquio A syndrome: anesthesiologists/anaesthetists, cardiologists, geneticists, neurosurgeons, oral surgeons, orthopedic surgeons, otolaryngologists, physical therapists/physiologists, pulmonologists, radiologists, etc.

In addition to monitoring changes in their patients' disease, the Morquio A syndrome-treating physician will have the opportunity to directly or indirectly coordinate care among the full team of specialists on whom their patients rely. Cervical myelopathy arising from atlantoaxial instability is of extreme concern in this patient population, and many non-specialist physicians who treat patients for either skeletal or non-skeletal Morquio A syndrome-related conditions may be unaware of the danger to the spinal cord posed by head and neck manipulations and the risk to the patient of subluxation and quadriparesis [12]. Cardiac and respiratory manifestations of Morquio A have an important impact on surgical risk in these patients.

Therefore, a panel of 10 multinational, multidisciplinary skeletal dysplasia or Morquio A syndrome specialists convened in Miami, FL on December 7 and 8, 2012. Specialties represented on the panel included genetics, metabolic pediatrics, neurosurgery, pediatric anesthesiology, neuroradiology, musculoskeletal radiology, and orthopedic surgery. The panel's goal was to develop consensus recommendations for early identification and effective management of spinal cord compression, for anesthesia and surgical best practices, and for effectual cardiac and respiratory management in patients with Morquio A syndrome.

The target audience for these recommendations includes any physician who may encounter a Morquio A syndrome patient, however doctors who do not have access to the full spectrum of specialists and resources needed to support patients with Morquio A syndrome should attempt to refer patients to a center that does. Physicians who manage Morquio A syndrome or comorbid conditions within specialty centers should review these expert panel recommendations and fully understand the implications of spinal cord instability for their own practices.

This expert panel strongly recommends that every Morquio A syndrome patient undergo all medical assessments, monitoring, and treatments at specialty centers with experience in lysosomal storage disorder management and with a broad network of specialists who can be incorporated into individualized treatment teams. Ideally, these specialty centers would start as the medical home for pediatric patients and continue to provide comprehensive care throughout adulthood.

2. Definitions

Consensus recommendations have been developed based upon expert clinical experience and available scientific evidence.

Expert panel-defined characterizations of spinal instability and cord compression:

1. Spinal instability may occur with or without evidence of spinal cord compression.
2. Spinal cord compression should be expected for most or all patients with Morquio A syndrome but at a wide spectrum of ages, possibly because of distinct Morquio A syndrome phenotypes which have yet to be described genotypically or fully characterized clinically.
3. Although spinal cord decompression for patients with Morquio A syndrome is often necessary at the craniocervical junction, decompression may also be required at multiple spinal cord locations.
4. Cord function, current instability, and the likelihood of future instability are multifactorial considerations when contemplating any surgical intervention. Assessment of cord function by both clinical exam and diagnostic imaging is essential.

3. Recommendations

Patients with Morquio A syndrome have multiple risk factors for myelopathy and paresis: spinal cord compression results from bony stenosis and thickening of soft tissue coupled with ligamentous laxity, deformity, odontoid hypoplasia and atlantoaxial instability. Surgical indications for decompression with or without fusion can be difficult to ascertain [17]. Historically, many physicians performed prophylactic decompression and fusion on young, asymptomatic patients with Morquio A syndrome to prevent cord compression [18,19]. Current

Table 1
Recommended routine and preoperative assessments for early identification and effective management of spinal cord compression in patients with Morquio A syndrome.

Evaluation	Frequency[a]	Notes
Medical history		
Ambulation [24]	At initial visit and yearly	• Community or household ambulation and types of aid if used
Assisted breathing [24]	At initial visit and yearly	• Use and use duration of non-invasive assisted breathing device
Previous surgeries [24]	At initial visit and yearly	• Indications, types, and outcomes
Musculoskeletal involvement	At initial visit and yearly	• Accident history • Medications • Posture, walking, standing and sitting pattern • Testing of weight bearing and balance • Joint range of motion • Limitations of daily activities • Photo or video documentation of disease progression
Clinical assessment		
Physical examination		
Standing height, sitting height, and length [24]	At initial visit and yearly	
Respiratory assessment		
Pulmonary function (spirometry) [24]	At initial visit and yearly or every two years, prior to surgery	• Beginning at age 6 [25] • Specify standing or sitting and try to get both to estimate diaphragmatic involvement • Perform yearly if history of snoring or other evidence of sleep related apnea • Alternatives: polysomnography for young children who cannot complete spirometry or oxygen saturation trace overnight at home
Cardiac assessment		
Echocardiogram [24]	At initial visit and yearly	• Before ERT, if ERT becomes available • Consider obtaining 5-chamber view to capture aortic insufficiencies that may develop as patient ages
Cardiac MRI	Prior to surgery	• Immediately if echocardiogram shows pathological findings • Yearly or every two years routinely as patient ages and tolerates the exam
Blood pressure in both arms	At initial visit and yearly	• Check both arms; vascular abnormalities may not equally effect both limbs
Functional exercise capacity		
6-minute walk test [26]	At initial visit and yearly	• Standardize as much as possible (day of week and time, inside or outside) to most accurately assess change over time [24]
3-minute stair climb [27–29]	At initial visit and yearly	• Consider replacing with Expanded Timed Get-Up and Go test, which may be less research-oriented, more repeatable, and more indicative of patients' daily activities [24,30]
Skeletal assessment		
Skeletal survey by radiography [24,31]	At initial visit; repeat when clinically indicated	• Routine annual survey not indicated • Attempt to collect historical radiographs
Neurophysiologic function		
Pinch and grip test [24]	At initial visit and yearly	• Consider Jamar® hand dynamometer • Some data for pinch and grip strength of Morquio A patients is available [32]
Neurological testing	At initial visit and yearly	• Muscle strength grading • Reflexes • Presence or absence of clonus • Babinski response
Deep tendon reflex assessment	At initial visit and yearly	
Proprioception (test for Romberg sign and position sense)	At initial visit and yearly	
Vibration sensation assessment in lower extremities	At initial visit and yearly	
Cognitive function and quality of life		
Muscular and neurologic pain assessment	At initial visit and yearly	
Developmental assessment, review of school performance	At initial visit and yearly	
Spinal assessment: instability and stenosis		
Radiograph of entire spine in prone position	At initial visit and yearly or every two years	
MRI of entire spine in supine position — T1 and T2 sequences	At initial visit and yearly or every two years	
When MRI is not available: AP and lateral radiograph of entire spine standing (or sitting when standing is not possible), including lateral radiograph of cervical spine in neutral position and in flexion–extension	At initial visit and yearly or every two years	
MRI of thoracolumbar spine in standing position	At initial visit; repeat when clinically indicated, prior to surgery	• Routine annual survey not indicated • Consider if suspicion of lower spinal cord compression
When MRI is not available: lateral radiograph of cervical spine in neutral position and in flexion–extension	At initial visit and yearly or every two years	• Pre-operatively and if high anesthetic risk • Without sedation in cooperative patients
MRI of cervical spine in flexion–extension	At initial visit and yearly or every two years	• The safest position for the patient is neutral • Sagittal T2 and axial T2 MRI in flexion–extension may yield helpful information prior to surgery, but testing the patient's limits of flexion and extension beforehand is essential
Spinal assessment: instability and stenosis		
Radiograph of entire spine in prone position	At initial visit and yearly or every two years	
MRI of entire spine in supine position — T1 and T2 sequences	At initial visit and yearly or every two years	

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Table 1 *(continued)*

Evaluation	Frequency[a]	Notes
Clinical assessment		
Spinal assessment: instability and stenosis		
When MRI is not available: AP and lateral radiograph of entire spine standing (or sitting when standing is not possible), including lateral radiograph of cervical spine in neutral position and in flexion–extension	At initial visit and yearly or every two years	
MRI of thoracolumbar spine in standing position	At initial visit; repeat when clinically indicated, prior to surgery	• Routine annual survey not indicated • Consider if suspicion of lower spinal cord compression
When MRI is not available: lateral radiograph of cervical spine in neutral position and in flexion–extension	At initial visit and yearly or every two years	• Pre-operatively and if high anesthetic risk • Without sedation in cooperative patients
MRI of cervical spine in flexion–extension	At initial visit and yearly or every two years	• The safest position for the patient is neutral • Sagittal T2 and axial T2 MRI in flexion–extension may yield helpful information prior to surgery, but testing the patient's limits of flexion and extension beforehand is essential
Pre-operative assessment		
Fiberoptic airway assessment [24]	Prior to surgery	• When respiratory symptoms are evident • For adults and children • Non-sedated if possible
Airway fluoroscopy	Prior to surgery	• If craniocervical CT unavailable consider bronchoscopy to assess broncho- or tracheomalacia
CT of the airway to carina	Prior to surgery	• If worsening lung function test or stridor • Perform at same time as cervical spine CT unless patient is sedated • May be reconstructed from previous CT series if lower level crosses carina
CT of the cervical spine from occiput to T4 in neutral. May consider flexion and extension if additional information is beneficial	Prior to surgery	• When symptomatic myopathy or prior to major, neurosurgical or orthopedic procedures • Sedation may be necessary to reduce movement for accurate 3D reconstruction of long spine segments
Radiograph of cervical spine in flexion and extension from occiput to T4. Consider AP and lateral of entire spine if more instrumentation is considered	At initial visit and yearly or every two years, prior to surgery	• Pre-operatively if neurosurgery or if the procedure will require the patient to be placed in prone position
Intra-operative assessment		
MEP and SSEP	During surgery	• During all neurosurgical procedures, especially those performed prone • Consider MEP/SSEP in awake, co-operative patients to determine operative position associated with lowest risk of cord compression
Invasive blood pressure monitoring	During surgery	• Arterial and central venous pressure monitoring for all major cases

[a] Tests should always be performed if and when clinically indicated, regardless of recommended frequency. Evaluations not listed in Table 1 should be performed as clinically indicated.

recommendations suggest decompression and fusion for asymptomatic patients should be performed when the space available for the cord is narrowed and cervical instability is present.

However, empirical values for a "narrowed" cord and "instability" differ among practitioners, and timing of surgical intervention is decided by a collection of clinical factors. Establishing numeric thresholds to describe compression is challenging for patients with mucopolysaccharidosis. Normal or average values for Torg ratios and space available for the cord (SAC) are difficult to determine because of the multifactorial causes of compression and the variability in presentation for this population. Measurements of a specific spinal region for the same patient can vary widely as well: patient positioning (sitting, standing, or prone; in neutral position or in hyperflexion) and the imaging procedure used (MRI with various imaging protocols) greatly influence the appearance of space for the cord and fluid around the cord within the spinal column. Therefore, regular patient examinations that establish a baseline and show change over time are essential for detection of neurological deterioration (Table 1) [12,20–23]. The MRI protocol should be as short as possible, especially for patients requiring sedation. Sagittal T2 images of the cervical tract in neutral position (and in flexion and extension when possible) are the most informative for evaluation of space available for the cord and for detecting signs of myelopathy; axial T2 images are essential because stenosis could be falsely estimated using sagittal imaging alone.

Any event that causes sudden flexion or extension of the neck, such as whiplash or a fall, or any procedure in which the head and neck are manipulated under anesthesia, risks injury to the spinal cord and can be life-threatening [23]. Pre-operative assessments are absolutely essential during all surgeries, including those for non-skeletal comorbidities (Table 1). Intra-operative monitoring is essential during spine surgery; for other surgeries, intra-operative monitoring may be beneficial depending upon the procedure. The consensus panel also suggested some best practices for surgery and anesthesia.

3.1. Patient evaluations

The evaluations listed below include recommendations that may not be useful or practical for all patients or available at all centers. Sparse evidence-based literature is available to support these recommendations, which are based on expert clinical opinion. The physicians comprising this panel have access to varied clinical tools, reimbursement, and patient support systems. These recommendations are intended to

1. establish baseline scores for features that may change over time
2. may indicate, especially when considered collectively, the need for surgical intervention for spinal cord compression and instability
3. assist with pre-operative preparation should emergency surgery of any type be required
4. assist with pre-operative assessment for procedures not involving the spine

4. Comparison of Morquio A recommendations

Table 2 compares recommendations for Morquio A evaluation type and frequency from four groups of experts. Although these groups share experts or experts from the same clinical practices, the types and frequencies of recommended evaluations sometimes differ. The Morquio A patient population, indeed all mucopolysaccharidosis populations, is small and heterogenous. Clinical trials are rare and involve small numbers of patients. Clinical evaluations used for research purposes do

Table 2
Comparison of recommended evaluations and evaluation frequency for patients with Morquio A devised by four groups of experts. The names of experts who participated in multiple groups are underlined.

Evaluation	2014: Charrow, Alden, Breathnach, Frawley, Hendriksz, Link, Mackenzie, Manara, Offiah, Solano, Theroux	2013: White, Braunlin, Duarte da Ponte, Goldberg, Hendriksz, Horovitz, Jones, Kim, Kishnani, Lampe, Lavery, Mackenzie, McBride, Mendelsohn, Ramlee, Valayannopoulos, Younis [24]	2013: Solanki, Martin, Theroux, Lampe, White, Shediac, Lampe, Beck, Mackenzie, Hendriksz Harmatz [23]	2012: Hendriksz, Al-Jawad, Berger, Hawley, Lawrence, McArdle, Summers, Wright, Braunlin [15]
Medical history				
Ambulation	At initial visit and yearly	At initial visit and yearly	–	–
Assisted breathing	At initial visit and yearly	At initial visit and yearly	–	–
Previous surgeries	At initial visit and yearly	At initial visit and yearly	–	–
Musculoskeletal involvement	At initial visit and yearly	–	–	–
Clinical assessment				
Physical examination				
Standing height, sitting height, and length	At initial visit and yearly	At initial visit and yearly	–	–
Respiratory assessment				
Pulmonary function (spirometry)	At initial visit and yearly or every two years; prior to surgery	At initial visit and yearly or every two years	–	At diagnosis and annually
Cardiac assessment				
Echocardiogram	At initial visit and yearly	At initial visit and yearly	–	At diagnosis and every 1–3 years and prior to surgery
Cardiac MRI	Prior to surgery	–	–	–
Blood pressure in both arms	At initial visit and yearly	–	–	–
Functional exercise capacity				
6-minute walk test	At initial visit and yearly	–	Should be performed	At diagnosis, annually, before and after surgery, and as clinically indicated
3-minute stair climb	At initial visit and yearly	–	–	At diagnosis, annually, before and after surgery, and as clinically indicated
Neurophysiologic function				
Pinch and grip test	At initial visit and yearly	At initial visit and yearly	–	–
Neurologic testing (muscle strength grading, reflexes, clonus, Babinski reflex assessment)	At initial visit and yearly	–	At diagnosis, every 6 months, and as clinically indicated	Physiotherapist should assess annually
Deep tendon reflex assessment	At initial visit and yearly	–	–	–
Proprioception (test from Romberg sign and position sense)	At initial visit and yearly	–	–	–
Vibration sensation assessment in lower extremities	At initial visit and yearly	–	–	–
Cognitive function and quality of life				
Muscular and neurologic pain assessment	At initial visit and yearly	–	–	Evaluation of impairment by physiotherapist at diagnosis, yearly, and before and after surgery
Developmental assessment, review of school performance	At initial visit and yearly	–	–	–
Pre-operative assessment				
Fiberoptic airway assessment	Prior to surgery	Prior to surgery or with symptoms	–	–
Airway fluoroscopy	Prior to surgery	–	If deemed necessary by pulmonologist	–
CT of the airway to carina	Prior to surgery	–	–	–
CT of the cervical spine from occiput to T4 in neutral. May consider flexion and extension with sedation if additional information is beneficial	Prior to surgery	–	CT neutral region of interest	–
Radiograph of cervical spine in flexion and extension from occiput to T4. Consider AP and lateral of entire spine if more instrumentation is considered.	At initial visit and yearly or every two years and prior to surgery	–	–	–
Pre-operative assessments discussed in previous sections	Urodynamic assessment/ cystometrogram, MEP, SSEP	–	–	Echocardiogram, auscultation, cardiac ultrasound, 6-minute walk test, 3-minute stair climb, and muscular and neurologic pain assessment
Skeletal assessment				
Skeletal survey by radiography	At initial visit	At initial visit	–	–
Spinal assessment: instability and stenosis				
Radiograph of entire spine	In prone position at initial visit and yearly or every two years	–	At time of diagnosis, every 2–3 years, and when clinically indicated	–

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Table 2 *(continued)*

Evaluation	2014: Charrow, Alden, Breathnach, Frawley, Hendriksz, Link, Mackenzie, Manara, Offiah, Solano, Theroux	2013: White, Braunlin, Duarte da Ponte, Goldberg, Hendriksz, Horovitz, Jones, Kim, Kishnani, Lampe, Lavery, Mackenzie, McBride, Mendelsohn, Ramlee, Valayannopoulos, Younis [24]	2013: Solanki, Martin, Theroux, Lampe, White, Shediac, Lampe, Beck, Mackenzie, Hendriksz Harmatz [23]	2012: Hendriksz, Al-Jawad, Berger, Hawley, Lawrence, McArdle, Summers, Wright, Braunlin [15]
MRI of entire spine in supine position — T1 and T2 sequences	At initial visit and yearly or every two years	–	Entire spine with attention to craniocervical junction at time of diagnosis and at regular intervals	–
When MRI is not available: AP and lateral radiograph of entire spine standing (or sitting when standing is not possible)	At initial visit and yearly or every two years	–	–	–
MRI of thoracolumbar spine in standing position	At initial visit and prior to surgery	–	–	–
Lateral radiograph of cervical spine in neutral position and in flexion–extension	At initial visit and yearly or every two years	–	AP and lateral cervical radiographs (including flexion–extension) at time of diagnosis and every 2–3 years if evidence of kyphosis or scoliosis	–
MRI of cervical spine in flexion–extension	At initial visit and yearly or every two years	–	At diagnosis, every 1–3 years, and when clinically indicated	–
Intra-operative assessment				
MEP and SSEP	During surgery	–	Total intravenous anesthesia (TIVA) is used to facilitate optimal capture of the potentials	–
Invasive blood pressure monitoring	During surgery	–	–	–

–, not discussed or not specifically recommended.

not necessarily accurately reflect patients' real-life limitations or disease manifestations. The scarcity of published, evidence-based medicine means that recommendations for the types and frequency of evaluations are necessarily based upon clinicians' experiences and best judgment. In addition, the standard of care rightly evolves as new evidence, evaluations, or procedures become available. The objectives among the four sets of recommendations differ as well, and therefore the types of evaluations or their frequencies may have been adapted to address the authors' specific goals.

4.1. Best practices

No “typical” patient with Morquio A exists, nor is any surgery for a Morquio A patient to be considered “routine”. Each surgical situation is unique, so several recommendations for anesthesia and surgery best practices to safeguard patients are listed below.

4.1.1. Anesthesia

1. An anesthesiologist who has experience with the difficult airways of patients with Morquio A syndrome should be the primary administrator of sedation or anesthesia for all procedures requiring anesthesia, including imaging and clinical evaluations.
2. Preoperative sedative premedication may reduce the risk of spinal cord injury occurring when an uncooperative patient struggles during anesthesia induction.
3. Difficult intubation should be expected and alternative airway devices should be readily available. Many patients with Morquio A syndrome younger than 20 years are not able to tolerate fiber optic intubation while awake and require sedation for intubation [33,34].
4. An assessment of the position of the cricothyroid membrane position should be made prior to anesthetic induction. If the cricoid is impalpable or retrosternal both an otolaryngologist and cardiac surgeon should be available for tracheostomy, cricothyroidotomy or upper median sternotomy in the event of a “can't ventilate, can't oxygenate” crisis.
5. Many manipulations of the patient's body during a surgical procedure can cause inadvertent compression of the cervical spine with the potential for temporary or permanent damage. Assigning one member of the operating team to stand at the patient's head for manual in-line stabilization may reduce the chance of cord damage from inadvertent cervical flexion.
6. Intra-operative anesthesia should allow continuous interpretation of SSEP or MEP and provide opportunity for wake-up tests with amnesia.
7. When possible after surgery, patients should be extubated while still in the operating room. If extubation is delayed and the patient is moved to intensive care, extubation should be managed by the same anesthesiologist or by an anesthesiologist with similar Morquio A syndrome expertise when possible; full access to equipment for the management of severe airway obstruction upon extubation should be available during recovery.
8. Whether or not the patient is extubated immediately after surgery, the patient should be awoken as soon as possible and asked to demonstrate movement of the lower extremities. Practicing these movements, such as toe-wiggling, with the patient prior to surgery can improve response time.
9. Be aware that tracheostomy in patients with Morquio A syndrome may be very difficult to perform.
10. Although epidural anesthesia has been performed successfully for patients with Morquio A syndrome [35], epidural anesthesia is not currently recommended for this group of patients. This change in practice is due to the recent cases of spinal cord infarction that occurred in Morquio patients following lower extremity surgeries where there was an epidural placed during surgery for post operative pain management [36]. Three such cases of spinal cord infarction occurred 12 to 36 h post-operatively and one additional case of infarction occurred in the operating room. This last case was different in that the surgery was Occiput-C1 fusion but the spinal cord infracted at upper thoracic levels [37].

4.1.2. Surgery

1. Patients with Morquio A syndrome who require surgery for any reason should be referred to a medical center that has a team of physicians with expertise in the management of Morquio A syndrome.

2. Intra-operative monitoring should begin while the patient is supine and then continue after the patient is prone.
3. Spinal surgery at any level is associated with a higher risk of spinal cord injury. Therefore, neurophysiological monitoring using SSEPs or MEPs during surgery to monitor spinal cord function is strongly recommended. Monitoring allows early identification of surgery- or anesthesia-induced neurophysiological changes, directs changes to cord perfusion and to surgical approach, and may prevent permanent damage and neurological deficit [38–41].
4. Neurophysiological monitoring may also be considered in patients undergoing procedures other than spinal surgery, particularly patients who are at increased risk of spinal cord compression, and for long procedures or procedures requiring head movement [42,43]. Spinal cord compression may also occur in the absence of clinical neurological symptoms and after several hours of surgery [43].
5. As the patient is transitioned from supine to prone, the pectus carinatum can create intrathoracic compression, particularly cardiac compression, respiratory excursion restriction, and abdominal compression, which affects venous return on diaphragmatic excursion. Neuropathy from compression is also possible. Working with the patient before anesthesia to modify the operating table with customized padding can help limit neuropathy from compression. Joint deformity may prevent traditional "in-line" positioning.
6. Flagging the chart of a Morquio A syndrome patient with a "spine at risk" statement will alert physicians who are performing incidental procedures at the same center to involve the patient's Morquio A syndrome treatment team.

5. Conclusion

Patients with Morquio A syndrome are at great risk of developing neurological deficits from cervical spinal cord compression and atlantoaxial instability. Patients with Morquio A syndrome are also likely to need additional fusion surgeries over time; up to 40% of patients who underwent fusion before age 36 months needed a second surgery within an average of about 8 years [44]. Continued surveillance is essential.

Patient assessments establish baseline values that can be monitored for change over time. The recommended assessments may indicate, especially when considered collectively, the need for surgical intervention for spinal cord compression and will serve as a foundation for preoperative preparation should emergency surgery of any type be required. Patients with Morquio A syndrome should be treated by specialists highly familiar with their disease and be referred to centers with multi-specialty Morquio A syndrome treatment teams for both skeletal and non-skeletal surgeries.

Author participation

The panel of specialists convened in Miami, FL on December 7 and 8, 2012 was chaired by Joel Charrow. The participants contributed equally to discussion and authors contributed equally to the manuscript review. Catherine Breathnach did not participate in the meeting discussion but prepared the manuscript.

Conflicts of interest

For this submitted work, the authors have received:

Authors	Conflicts of interest
All	Consulting fee or honorarium
All	Support for travel to meetings
All except Breathnach	Provision of writing assistance or administrative support
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