Journal of Research and Practice on the Musculoskeletal System JRPMS

Review Article

Neuromuscular Scoliosis: A Narrative Review

Nikolaos Dimitrakis[1,2], Christos P. Zafeiris[2,3]

[1]*Department of Orthopaedic Surgery, Asklepieio Voulas, Athens, Greece;*
[2]*Postgraduate Program "Metabolic Bone Diseases", National and Kapodistrian University of Athens, Medical School, Athens, Greece;*
[3]*Laboratory for the Research of the Musculoskeletal System "Th. Garofalidis", National and Kapodistrian University of Athens, Medical School, Athens, Greece*

Abstract

Spinal deformity is a common finding in patients with an underlying neurological disorder. The clinical course of patients with neuromuscular scoliosis depends on the nature, severity, and the overall impact of their neuromuscular disease. Progressive spinal deformity causes difficulty in mobility and seating status, and may be associated with cardiac and pulmonary complications. Management of neuromuscular scoliosis requires a multidisciplinary approach to obtain the best possible outcome. It is essential for patients to understand the nature of neuromuscular scoliosis, the potential risks and benefits of operative and nonoperative interventions. In this review, we discuss the causes, evaluation and management -both operative and nonoperative- of neuromuscular scoliosis.

Keywords: Cerebral palsy, Duchenne muscular dystrophy, Neuromuscular scoliosis, Spinal deformity, Spinal muscular atrophy

Introduction

The term "scoliosis" is derived from the Greek word "scolios", meaning "curved" or "crooked". Scoliosis is a multifactorial three-dimensional deformity of the spinal column, which is characterized by lateral inclination of at least 10 degrees of the spinal column, combined with rotational deformity of the vertebrae and in the vast majority of the cases, reduction of the physiological kyphosis of the spine with hypo-lordosis in the lumbar portion and hyper-lordosis in the lumbo-sacral portion of the spinal column[1].

Scoliosis has been the subject of concern by the medical community for thousands of years; in 3.500 BC, ancient Hindu texts describe the case of a woman whose back was deformed in three separate areas, and required the intervention of the god Krishna in order to get it straight, by placing his feet on hers and simultaneously pulling her by the chin. Hippocrates, the Ancient Greek doctor, mentions in his writings that he was trying to treat the patients with scoliosis through application of traction. The actual revolution in the treatment of the disease began in the 16th century, with the use of the first scoliosis braces by Pare in 1511. In the first years of the 20th century, Hibbs introduced the surgical techniques of posterior spinal fusion in order to restore the deformity of the scoliotic spinal column, while much later, Hurrington used the techniques of internal fixation with rods and screws[2].

Scoliosis can be classified into three major categories[3]:

1. Congenital scoliosis: may be due either to failure of formation of part of the spine (eg, a hemivertebra, which is the most common anomaly producing congenital scoliosis), or failure of segmentation (ie, a block vertebra). The pathology is congenital disorders either of the musculoskeletal system (eg muscular dystrophy or arthrogryposis), or of the nervous system (dysautonomia, motor neuron disease).
2. Idiopathic scoliosis: It accounts for around 80% of scoliosis cases. The etiology of idiopathic scoliosis is unknown and presumably multifactorial. It is divided further into

The authors have no conflict of interest.

Corresponding author: *Nikolaos Dimitrakis, Department of Orthopaedic Surgery, Asklepieio Voulas, Athens, Greece*

E-mail: *nikdimitrakis@gmail.com*

Edited by: *Konstantinos Stathopoulos*

Accepted *1 August 2022*

Infantile (age of onset 0-3 years), Juvenile (age of onset 3-10 years) and Adolescent (age of onset 11 and older, or from onset of puberty until skeletal maturity).

3. Secondary scoliosis: although this type is very rare, it can be caused by several pathologic conditions, including disorders of the nervous system (spinal cord tumors, syringomyelia, neurofibromatosis, Friedreich's ataxia), of the connective tissue (Ehlers-Danlos syndrome, Marfan's syndrome, homocystinuria), or disorders of the musculoskeletal system (injuries or fractures of the spinal column, congenital dislocation of the hip joint, osteogenesis imperfecta, Klippel-Feil syndrome).

Neuromuscular scoliosis is defined as a non-congenital scoliotic deformity that occurs in patients with any type of pre-existing neuromuscular diagnosis[4]. Neuromuscular scoliosis can occur at any age and causes significant morbidity and impairment of patients' daily living functionality, while simultaneously deteriorating their health-related quality of life.

Etiology of neuromuscular scoliosis

According to the Scoliosis Research Society[5], neuromuscular scoliosis is classified into two major groups: neuropathic pathological conditions and myopathic pathological conditions. The further categorization of these two large groups is the following:

1. **Neuropathic conditions**

Upper motor neuron lesions
- Cerebral palsy
- Spinocerebellar degeneration (Spinocerebellar ataxia, Roussy-Levy disease, Friedreich ataxia)
- Spinal cord trauma
- Spinal cord tumor
- Syringomyelia

Lower motor neuron lesions
- Poliomyelitis and other viral myelitides
- Trauma
- Charcot – Marie – Tooth disease
- Spinal muscular atrophy (type 1: Werdnig – Hoffmann disease, and type 2: Kugelberg – Welander disease).
- Dysautonomia (Riley – Day syndrome).

Combined upper and lower motor neuron lesions
- Tethered spinal cord
- Myelomeningocele
- Amyotrophic lateral sclerosis

2. **Myopathic conditions**
- Muscular dystrophy (Duchenne's muscular dystrophy, Facioscapulohumeral dystrophy, Limb – girdle dystrophy
- Congenital hypotonia
- Myotonic dystrophy
- Arthrogryposis

Due to the fact that neuromuscular scoliosis has many causes, the patterns and incidence differ greatly. The incidence of spinal deformity in patients with a neuromuscular disorder is much higher than that in the general population. Generally, the greater the neuromuscular involvement, the greater the incidence, progression and severity of scoliosis (Table 1)[5,6]:

Neuromuscular disorders	Incidence of scoliosis
Cerebral palsy, involving two limbs	25%
Cerebral palsy, involving four limbs	80%
Lower lumbar myelodysplasia	60%
Thoracic level myelodysplasia	100%
Spinal muscular atrophy	67%
Friedreich's ataxia	80%
Duchenne's muscular dystrophy	90%
Spinal cord injury, before skeletal maturity	100%

Table 1. The incidence of scoliosis in patients suffering from neuromuscular disorders[5,6].

Diagnosis and assessment of the patients with neuromuscular scoliosis

Evaluating patients with scoliosis with suspicion of neuromuscular origin, is essential, not only to make an accurate diagnosis of their underlying neuromuscular disease, but also to determine accurately the limitations and the functional impairments caused by the deformity of their spinal column[7]. A detailed patient's history should be documented, including the perinatal period, the family history, the various milestones of their development, the presence of other pathologic conditions, with emphasis on renal and cardiac diseases and the exact age of the occurrence of the spinal deformity. During the initial assessment it is very crucial to distinguish the static pathological conditions and etiologies of neuromuscular scoliosis, such as myelomeningocele or cerebral palsy, from the gradually progressing and worsening pathologies (for example Duchenne dystrophy or spinal muscular atrophy). In addition, the age of the onset of the spinal deformity should be recorded in detail, in order to differentiate neuromuscular scoliosis from adolescent idiopathic scoliosis, which, in the vast majority of cases occurs at an older age[8].

Curve magnitude (Cobb angle measurement), pelvic obliquity, asymmetry of the shoulder girdle and the possible deformities of the ribs and the hip joint should be thoroughly examined. A complete neurological examination might reveal the presence of pathological reflexes, positive Babinski sign and Beevor sign (indication of paralysis or weakness of the rectus abdominis muscle due to injury of the spinal cord at the level of T10-T12)[9]. Hyporeflexia is a general indication

of lesions of the lower motor neuron (myopathy, neuropathy, spina bifida), whereas hyperreflexia indicates upper motor neuron pathology (cerebral palsy, vascular stroke or brain trauma, and injury of the spinal cord)[7].

In all cases, radiological control (both standing and seated X-ray views) is essential not only to make an accurate assessment of patients' condition but also to obtain indications regarding the progress of the disorder. As a general rule, left-sided scoliotic curves, very large ones and rapidly progressing ones should raise the suspicion of neuromuscular etiology of the scoliosis[10]. Imaging of the spinal cord with MRI will provide further information regarding the intraspinal pathology, such as the presence of lipomas or other tumors, syringomyelia, or tethered spinal cord.

Finally, in all cases, patients should be thoroughly assessed for the presence of congenital disorders in all body systems, especially the urinary tract and the heart as part of a concomitant syndrome; nevertheless, in most cases, congenital syndromic scoliosis is related to the pathology of the musculoskeletal system (especially the bones) and not to neuromuscular pathology[11].

Causes of neuromuscular scoliosis

Cerebral palsy

Cerebral palsy (CP) is a non – progressive encephalopathy, that occurs during the first 24 months of the life of the child, leading to neurologic deficits and various degrees of motor disturbance[12]. Persson-Bunke et al., (2012)[13] published an epidemiological study in order to describe the prevalence of scoliosis in children suffering from CP. The authors analyzed a population of 666 children with an age range between 4 and 18 years, in Sweden, of which 192 (28.8%) had some degree of scoliosis. 116 of them (17.5%), were characterized as having mild scoliosis and 76 (11.5%) were characterized as moderate or severe. In the majority of the cases, the diagnosis was made after the age of 8 years. Another important finding was the direct correlation between the severity of the cerebral palsy, as this is expressed according to the Gross Motor Function Classification System Level (GMFCS)[14]: patients who were categorized in levels IV and V according to the GMFCS had more than 50% probability developing moderate or severe neuromuscular scoliosis, whereas patients in the I and II level had minimal risk.

In another cross-sectional descriptive study, Bertoncelli et al., (2017)[15], tried to identify the risk factors that lead children with cerebral palsy to develop severe forms of neuromuscular scoliosis. The factors which were found to have statistical significance were:

- Severe epilepsy,
- Levels IV and V in the GMFCS,
- History of surgery of their hip joint,
- Severe spasticity of their limbs,
- Non-ambulatory children and
- Female gender.

An additional important finding in children with cerebral palsy is that in those cases where scoliosis exceeds 40°, continuous progression and deterioration should be expected, even at a rate of 2°/month, irrespective of scoliosis brace use. Long, collapsing C-type scoliotic curves are found in children with whole-body CP, hypotonic children usually develop hypo-kyphosis, whereas children with CP in whom the main feature of the disorder is athetosis and/or dystonia, usually present with milder forms of scoliosis[16].

Duchenne muscular dystrophy

Duchenne muscular dystrophy is a severe form of muscular dystrophy, affecting mainly the male gender since it is an X-linked recessive disorder and is caused by a mutation of the gene which codes protein dystrophin. In addition, it is thought that about 1/3 of the cases are caused by a new mutation of the gene, rather than its inheritance[17]. In most cases, the diagnosis is made by the age of 2-3 years, with the scoliosis being mild by that time and progressing more rapidly as soon as the children lose their mobility and confine in a wheelchair. Chronic administration of glucocorticoids has been one of the main treatment options, stabilizing muscle strength and slowing its decline; Alman et al., (2004)[18], in a non-randomized controlled study, showed that steroid treatment slowed the progression of scoliosis in young boys (7-10 years old) suffering from Duchenne muscular dystrophy, reducing the incidence of surgery from 64% in the control group to 16% in the treatment group (deflazacort), after 5 years follow-up.

Spinal muscular atrophy

Spinal muscular atrophy (SMA) is a rare neurodegenerative disorder, caused by a mutation of the SMN1 gene and inherited in an autosomal recessive manner[19]. SMA is characterized by progressive motor and respiratory muscle weakness. There are five main types of the SMA: SMA 0 (prenatal), SMA1 (Werdnig-Hoffmann disease, 0-6 months), SMS2 (Dubowitz disease, 7-18 months), SMA3 (Kugelberg-Welander disease, >18 months) and SMA4 (adult-onset disease). The fundamental problems for patients with SMA type 2 and 3 are the reduced pulmonary function, and progressive scoliosis (collapsing C-type scoliotic curves) with increasing pelvic obliquity. On the other hand, children who are able to walk have a lower incidence of scoliosis, which appears at an older age (older than 10 years old) and is relatively mild[20].

Myelomeningocele

Myelomeningocele is the fourth and most severe form of spina bifida: it occurs when the spinal cord and/ or some of its nervous elements are exposed through an opening in the patient's spinal column, resulting in partial or total paralysis, along with severe sensory disturbances distal to the level of the spinal opening. This paralysis may be so severe that the patient cannot walk and simultaneously suffer from severe

bowel and urinary dysfunction[21]. Scoliotic deformities presence in conjunction with myelomeningocele possess a significant challenge for the treating physician, since they are accompanied by a complex series of pathologic conditions which include[22]:

- Severe and in multiple planes deformity of the patient's spinal column, accompanied in most of the cases by congenital defects of the vertebrae,
- Abnormal anatomy of the affected vertebral pedicles,
- Subcutaneous location of the dura,
- A large number of coexisting serious pathologic conditions, such as Chiari malformation, hydrocephalus, contractures of the patient's lower limbs, tethered spinal cord along with neurogenic bladder and bowel
- The insensate skin distally to the level of the myelomeningocele.

Because of all the above pathological conditions, the use of a scoliosis brace, especially in the cases where the spinal deformity is progressing, could be a very complex task. In addition, the obliquity of the pelvis in conjunction with the insensate skin most of the time leads to the formation of pressure sores in the affected areas; pressure sores and skin breakdown can also occur on the curve's apex. It is therefore a very complex condition to treat, either conservatively or surgically, and most of the time requires cooperation with other surgical specialties, such as plastic surgeons[23].

Management of neuromuscular scoliosis

Nonoperative management

In the vast majority of the patients with neuromuscular scoliosis, initial treatment is conservative; however, its effects are limited, as the use of spinal braces does not seem to have a clinically significant effect on the progression of the scoliotic curves, acting only as an external postural support which assists patients in maintaining sitting position and improving muscle balance[4]; in addition, severe deformity of the spine leads to the collapse of the trunk, making almost impossible to accept the hard materials used in most of the orthotic devices[24]. Nakamura et al., (2014)[25] published the results of a pilot prospective study in 54 patients with neuromuscular scoliosis (mainly cerebral palsy patients), with mean age of 10 years (range 2-18 years), who were treated with a three-point support orthotic device, called "dynamic spinal brace" – (DSB). The results of the study showed that patients' compliance with the brace was good; its main advantage was the support and the improvement of the patients' sitting balance, without being particularly effective in improving or at least maintaining the spinal deformity. Also, the study showed that the DSB was more effective for the treatment of long C-curve scoliotic patterns rather than short patterns.

Even the custom-made braces used to treat severe cases of neuromuscular scoliosis had several disadvantages, such as the complicated manufacturing process, the high cost, and the fact that in many cases, when delivered to the patients the deformity has already progressed and was no longer fitting adequately to them[4].

The optimal strategy is to treat the patient with neuromuscular scoliosis with a brace when the scoliotic curve is relatively small (<25°) and flexible, informing the family and the caregivers that the main goal of the conservative treatment is to improve the patient's balance, positioning and overall function, but not improve the spinal deformity itself, which will, most probably, continue to progress[26]. In all cases, continuous monitoring and periodic assessment of the patient's condition with the attempt to treat or at least control the primary cause of the deformity is necessary. Lebel et al. (2013)[27], showed that long-term glucocorticoid treatment in boys with neuromuscular scoliosis due to Duchenne muscular dystrophy resulted in a statistically significant decrease in the need for operative treatment of their scoliosis. Another important measure for all the patients with neuromuscular scoliosis who mobilize with the use of a wheelchair is the proper wheelchair modification in order to adapt and optimize its construction along with the continuous growth of the patient's spine[7].

Operative management

The decision and the indications for the surgical treatment of a patient with neuromuscular scoliosis are complex and multifactorial and, in all cases, should be made after a detailed discussion and agreement with the patients and their families. As a general rule, surgery should be performed in patients in whom the degree of the deformity is so severe that it greatly impairs their overall function as well as their quality of life: among these important clinical and functional disorders are the following[16]:

- Poor sitting balance,
- Chronic pain of the back and/or the costo-pelvic region,
- Complications from the respiratory system,
- Severe functional problems regarding feeding and self-care of the patients.

In cases where scoliosis exceeds 40°, it should be expected that it will further progress; furthermore, surgical treatment of severe scoliotic curves (>90°) is accompanied by a high probability of serious perioperative and postoperative complications, while the final outcome might be unsatisfactory. Two are the main surgical techniques for neuromuscular scoliosis[28]:

1. Growth preserving techniques: the main indications for this type of surgical technique include early-onset neuromuscular scoliosis (before the age of 10 years), in hypotonic and non-ambulatory patients, suffering predominantly from myopathic conditions; the primary goal of the procedure is to control the spinal deformity, preserving its growth along with the development of the chest so as to delay the definite spinal fusion as long as possible. The main techniques of this category include the modern self-growing Luque trolley technique and the Shilla

technique, which involves instrumental fusion of the apex of the deformity along with the use of non-locking screws distally and proximally, with the telescoping rods left long to accommodate the spinal growth in the longitudinal axis[29]. Recently, Miladi et al., (2018)[30] published the results of a novel fusionless, minimally invasive technique based on the use of a bilateral double rod sliding construct; they applied this technique to 100 patients (mean age 11 years) suffering from neuromuscular scoliosis (cerebral palsy, SMA, muscular dystrophy and other neurological conditions). The results, after a mean 3 years follow-up were promising, achieving adequate correction of the spinal deformity and the pelvic obliquity while reducing the complication rate in comparison to the previously mentioned surgical techniques.

2. Spinal fusion: The main objective of these techniques is to ensure a solid bony fusion of the patient's spine, preventing the progression of the deformity, while correcting as far as possible the spinal and pelvic deformity and restoring the standing or the sitting balance of the patient. In the vast majority of the cases in order to achieve those goals, posterior fusion of the spinal column is required, whereas there are only sporadic reports for the use of anterior fusion techniques (for example in cases of myelomeningocele, where there is poor soft tissue coverage of the posterior elements of the spinal cord)[22,31]. In very rare severe cases with severe and rigid deformity, combination of posterior with anterior spinal fusion can be used, taking into account the high morbidity and mortality rates associated with this procedure. The use of continuous intraoperative spinal cord monitoring in ambulatory children can be very useful, along with the recording of cervical somatosensory evoked potentials in patients with myopathic pathologies.

In all the cases of patients undergoing surgery for neuromuscular scoliosis, the surgeon should be aware that the complication rates are significantly higher compared to the surgical procedures performed for idiopathic scoliosis. Reames et al., (2011)[32], after reviewing 19.360 cases of pediatric scoliosis treated between 2004-2007, reported 17.9% complication rates for neuromuscular scoliosis, 10.6% for congenital scoliosis and 6.3% for idiopathic scoliosis; idiopathic and congenital cases had the same mortality rate (0.3%), more than 10 times higher than the idiopathic ones (0.02%). Also, anterior procedures were related to higher rates of producing new neurologic deficits in comparison to the posterior – pedicle screw procedures.

Conclusions

Neuromuscular scoliosis is a particularly difficult pathologic condition to treat, since it is associated with numerous comorbidities which must be all taken into account before, during and after treatment. For the successful treatment of this condition, the collaboration of a multidisciplinary team of health professionals is necessary, including physicians from multiple medical specialties, along with allied professionals, such as physiotherapists, occupational therapists, wheelchair technicians, and even psychologists.

Even though the initial therapeutic approach is mainly conservative, if patients' clinical condition deteriorates very quickly, affecting significantly their quality of life, surgical treatment should be considered while taking into account the high rates of complications, morbidity, and postoperative mortality. Modern posterior instrumentation surgical techniques which have been developed in recent years provide the ability to satisfactorily correct spinal deformity, with a reduction of the number of complications. At all stages of the therapeutic interventions of neuromuscular scoliosis full cooperation with the patients and their families is essential in order to achieve the best possible results and always have realistic expectations.

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