Surgical Treatment and Outcomes of Scoliosis and Cervical Spine Instability in Children

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MARULLO
Ah! ah! Rigoletto... Caso enorme!
CORO, BORSA
Perduto ha la gobba? non è più difforme?

Rigoletto, Giuseppe Verdi

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List of Original Publications

1. **Mattila M**, Jalanko T, Helenius I. En Bloc Vertebral Column Derotation Provides Spinal Derotation but No Additional Effect on Thoracic Rib Hump as Compared with No Derotation in Adolescents Undergoing Surgery for Idiopathic Scoliosis with Total Pedicle Screw Instrumentation. Spine 2013;38:1576-83.

2. **Mattila M**, Jalanko T, Puisto V, Pajulo O, Helenius I. Hybrid versus total pedicle screw instrumentation in children undergoing surgery for neuromuscular scoliosis: A comparative study with matched cohorts. J Bone Joint Surg Br 2012;94:1393-8. §

3. Helenius I, **Mattila M**, Jalanko T. Morbidity and radiographic outcomes of severe scoliosis of 90° or more: a comparison of hybrid with total pedicle screw instrumentation. J Child Orthop. 2014;8:345-52. *

4. Pakkasjarvi N, **Mattila M**, Jalanko T, Remes V, Helenius I. Upper cervical spine fusion in children with skeletal dysplasia. Scand J Surg 2013;102:189-96. *

§ Publication is part of Tuomas Jalankos dissertation
* The authors contributed equally to the study

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Abbreviations

AIS	Adolescent idiopathic scoliosis
ALL	Anterior longitudinal ligament
AP	Anteroposterior
C1	First cervical vertebrae
C2	Second cervical vertebrae
CD	Cotrel-Dubousset instrumentation
Cobb angle	Angle of scoliosis lateral curvature
DVR	Direct vertebral rotation
en Bloc	Multi-vertebral block
EOS	Early-onset scoliosis
FVC	Forced vital capacity
JIS	Juvenile idiopathic scoliosis
N-DVR	Without direct vertebral rotation
NMS	Neuromuscular scoliosis
PFT	Pulmonary function test
PL	Posterolateral
PLL	Posterior longitudinal ligament
PSI	Pedicle screw instrumentation
SED	Spondyloephyseal dysplasia
SPO	Smith-Peterson osteotomy
SRS-24	Scoliosis Research Society 24 questionnaire
TIS	Thoracic insufficiency syndrome
TPS	Total pedicle screw
VEPTR	Vertical expandable prosthetic titanium rib

Abstract

Structural changes in the spine are the most common children's musculoskeletal abnormalities, as they cover 70% of all musculoskeletal disorders in children and adolescent. Idiopathic scoliosis is the most common of these structural changes. The congenital structural problems of the spine form an entity of their own. Changes in the development of the spine during fetal period range from changes in individual vertebral to being part of a wider developmental disorder. Careful follow-up and research are the basis of care. Genetically induced syndromes form a wide heterogeneous group that have vertebral problems often seen in cervical development and growth. There are a number of rare diseases in this group.

One of the primary aims of this thesis was to assess whether *en bloc* vertebral column derotation provides an efficient control or correction of thoracic rib hump as compared with no derotation in adolescents with an idiopathic scoliosis. The outcomes of hybrid and total pedicle screw instrumentation were compared in children undergoing surgery for neuromuscular scoliosis or severe scoliosis. Within the rare bone dysplastia group, we studied the outcomes of upper cervical spine fusion in this heterogeneous group.

We showed that *en bloc* derotation provides an effective initial correction of the rib hump, but the effect diminishes during two year follow-up.

Comparing hybrid technique with total pedicle screw method we proved that surgery with pedicle screw technique is more effective in correcting neuromuscular and severe scoliosis. Blood loss was significantly smaller (2000 ml) and patients had better major curve correction (two year follow-up 75% vs 59%) with less need for anteroposterior surgery when comparing these techniques in the neuromuscular group. Pedicle screw instrumentation provided shorter operative time (1 hour 39minutes), diminished blood loss (1600ml), enabled better major curve correction (73% vs 59%) with less need for anteroposterior surgery as compared with hybrid constructs in patients with severe over 90 degrees scoliosis.

Feasibility of different techniques were investigated in the rare disease group. Cervical spine instability in the patients with rare bone dysplasia surgery was found effective. Although results are encouraging , risks and complications are common.

Surgery has become an important part of treatment in many types of spinal disorders. Better techniques evolve from old methods and procedures only if these are studied meticulously.

Keywords: scoliosis, pedicle, rib hump, total pedicle screw technique, coronal balance, sagittal balance, rare bone dysplasia, cervical spine

Tiivistelmä

Lasten tuki- ja liikuntaelinten poikkeavuuksista ovat selkärangan rakenteelliset muutokset yleisimpiä. Ne edustavat noin 70 % kaikista lasten tuki- ja liikuntaelinten poikkeavuuksista. Idiopaattinen eli itsesyntyinen skolioosi on näistä yleisin ja sen kliiniseen kuvaan liittyy yhtenä löydöksenä kylkikohouma.

Kehitysviiveet muodostavat oman heterogeenisen ryhmän, jota kutsutaan neuromuskulaariseksi skolioosiksi. Synnynnäiset rakenteelliset selkärangan poikkeavuudet muodostavat oman ryhmänsä. Nikamien kehityksessä sikiökaudella tapahtuvat muutokset voivat olla yksittäisiä nikamamuutoksia tai osa laajempaa kehityshäiriötä. Geneettisesti ohjautuvat syndroomat muodostavat harvinaissairauksien heterogeenisen ryhmän, jossa selkärangan ongelmat usein painottuvat kaularangan kehitys- ja kasvuhäiriöihin.

Tässä väitöskirjatyössä haluttiin osoittaa, että idiopaattisen skolioosin kylkikohouman korjaamisessa käytetty tekniikka on tehokas, ja arvioida seurannassa miten pysyvä muutos on. Neuromuskulaaristen skolioosien hoidossa yleisesti käytetyn hybridileikkaustekniikan muuttamista pelkästään pedikkeliruuveja käyttävään tekniikaan haluttiin selvittää. Tämän pedikkeliruuvitekniikan hyötyä haluttiin arvioida myös isojen skolioosimutkien korjaamisessa. Harvinaisten luustodysplasia potilaiden hoidossa korostuvat kaularangan rakenteelliset ongelmat. Näiden potilaiden kaularangan rakenteet ovat pieniä ja heikkorakenteisia. Selvitimme kaularangan luudutusleikkauksia tässä heterogeenisessä ryhmässä.

Osoitimme tutkimustyössämme, että kylkikohouman korjaaminen on tehokas en bloc menetelmällä, mutta kylkikohouman korjausvaikutus pienenee seurannassa.

Vertaamalla hybriditekniikkaa ja vain pedikkeliruuveja käyttävää menetelmää osoitimme, että sekä neuromuskulaarisen skolioosien, että suurten skolioosimutkien hoito onnistuu paremmin pedikkeliruuvitekniikalla. Verenvuoto oli merkittävästi pienempi (2000ml), potilaiden skolioosin korjaus oli parempi (75% vs 59%) ja tarvitsivat vähemmän selkärangan etuosan kirurgiaa, kun verrattiin näitä ryhmiä neuromuskulaaristen potilaiden ryhmässä. Pedikkeliruuvitekniikka lyhensi leikkausaikaa (1 tunti 39 min), vähensi verenvuotoa (1600ml), tuotti paremman lopputuloksen skolioosin korjaukseen (73% vs 59% korjaus lähtötilanteeseen) ja vähensi selkärangan etuosan kirurgian tarvetta, kun hybridi ja pedikkeliruuvitekniikka verrattiin vaikeiden yli 90 asteen skolioosien ryhmässä.

Eri tekniikkojen soveltuvuutta kaularangan rakenneongelmien hoidossa tutkittiin harvinaissairauksien ryhmässä. Osoitimme että luustodysplasia potilaiden epävakaisen kaularangan hoidossa kirurginen hoito on tehokasta. Vaikka tulokset ovat rohkaisevia, niin riskit ja ei-toivotut tapahtumat ovat yleisiä.

Leikkaustekniikat kehittyvät vanhojen menetelmien pohjalta. Kirurgia kehittyy vain, jos edellisen sukupolven tekniikkoihin liittyviä ongelmia tutkitaan, heikkouksia korjataan ja menetelmiä kehitetään.

Avainsanat: skolioosi, nikamajalka, kylkikohouma, vain pedikkeliruuvitekniikkaa käyttävä tekniikka, etusuunnan tasapaino, sivusuunnan tasapaino, harvinaiset luustodysplasia sairaudet, kaularanka

1. Introduction

Scoliosis is by far the most common pediatric spinal disorder. Scoliosis is a multidimensional disease. Beginning from the two-dimensional view, we have slowly shifted to 3-dimensional thinking, as it provides more insights on the severity and progression of the deformity. Multidimensional imaging and classification are most beneficial for the evaluation of individuals with idiopathic scoliosis. Measuring all three dimensions and classifying them uniformly is challenging, but new technology provides tools for more accurate classification. (Donzelli et.al., 2015, Diebo B et al. 2019).

The history of surgical treatment for pediatric spinal disorder displays both the general evolution in our understanding of spinal biomechanics and the possibilities enabled by technological advances in surgical techniques. Initially, the goal of surgical treatment for scoliosis was to stop the progression of spinal deformity (Hibbs 1911, Harrington 1962). The advent of pedicle screw technique brought along more rigid fixation and consequently better ability to correct side translation, hypokyphosis, and rotational deformity of the spine. The surgical correction of scoliosis evolved from a simple strut graft retardant operation (Hibbs 1911) into corrective procedures that now includes full three dimensional dominance with a rigid construct. Today, our treatment strategy has evolved from effective correction of coronal balance (Suk et al. 1995) to understanding that correction of sagittal balance and pelvic posture related to deformity correction are equally important (Roussouly P, Nnadi C, 2010; Harding IJ, 2009). Unfortunately, the evolution of surgical technique has brought along new problems such as junctional problems, which are believed to be related to rigid correction (Helgeson MD et.al., 2010).

Adolescent idiopathic scoliosis (AIS) has gained probably most from the evolution of the surgical techniques over the past two decades. Better correction of spinal deformities has encouraged the surgeons to start treating patients with more severe deformities and follow-up studies have shown good clinical, radiographic, and quality of life outcomes (Danielsson et al. 2001; Helenius et al. 2008). The absolute significance of rotational deformity correction in spinal surgery is still uncertain. Limited evidence exists on the long-term outcomes of rotational correction (Rushton P et.al.2014). Rib hump correction remains the main concern in patients with adolescent idiopathic scoliosis, but thus far we have limited knowledge how the direct vertebral column derotation (DVR) affects the rib hump correction if thoracoplasty is not performed (Rushton, 2014). In contrast, the outcomes of surgery for neuromuscular scoliosis are less compelling. Patient related outcome studies remain still the cornerstones of modern scoliosis surgery. (Sibinski M et.al. 2013)

Different syndromes create cervical instability both in the upper and lower part. Upper cervical instability is typical of Down syndrome, while subaxial cervical instability is typical of Larsen and diastrophic dysplasia skeletal dysplasias (Campbell RM 2009; Remes et al. 1999, 2000). Unstable cervical spine produces a subtle threat particularly in patients with skeletal dysplasia (MacKenzie et al. 2013, 2015; Helenius et al. 2015) or Down syndrome (El-Khouri M, 2014).

2. Review of the Literature

2.1. Anatomy and function of Human Spine

Spine is complex synthesis of vertebras, ligaments, muscles and neural elements supporting the entire body weight and transmitting power to lower extremities. Spine is fundamental in sustaining balance, upright posture and supports chest cavity and respiration. Spine has the most delicate neural elements embedded with in a bony cavity called spinal canal.

Normal spine contains 7 cervical, 12 thoracic and 5 lumbar vertebras, combined with 5 sacral and 4 coccygeal vertebras. This complex structure of elements, one on top of another, has not only supporting function but is also flexible and adapts to the various needs of the spine, including the keeping of balance in various body positions.

The basic element of the spine is the vertebra. It consists from three primary structures: body, pedicles and posterior parts. (Sobotta Atlas of Human Anatomy, Volume 1 and 2)

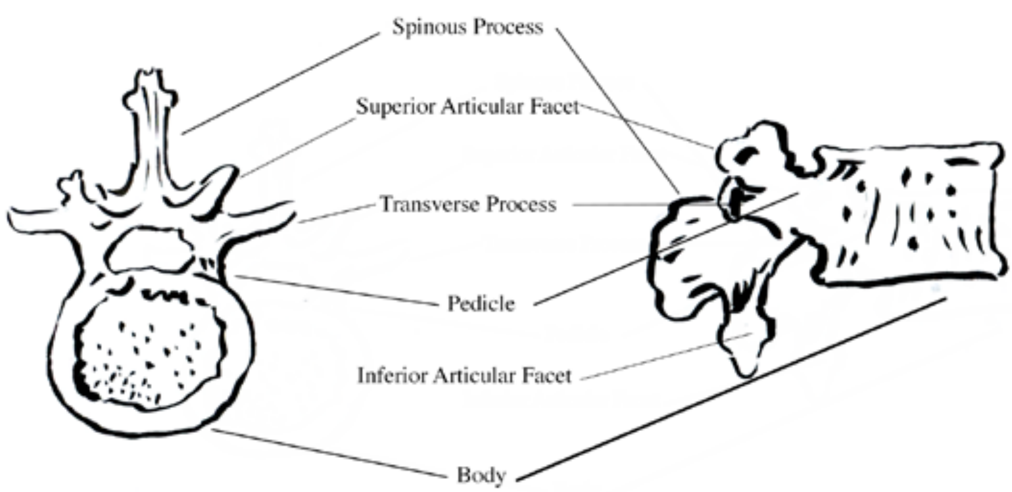

Figure 1. Lumbar Vertebra

Normal spine is straight when viewed at the coronal plane, while the sagittal plane has three curves; the lumbar lordosis, the thoracic kyphosis and a small cervical lordosis. A balanced spine lies under the head with the 7th cervical vertebra positioned directly above the sacrum in the coronal plane and above the femoral heads in the sagittal plane. (Figure 2).

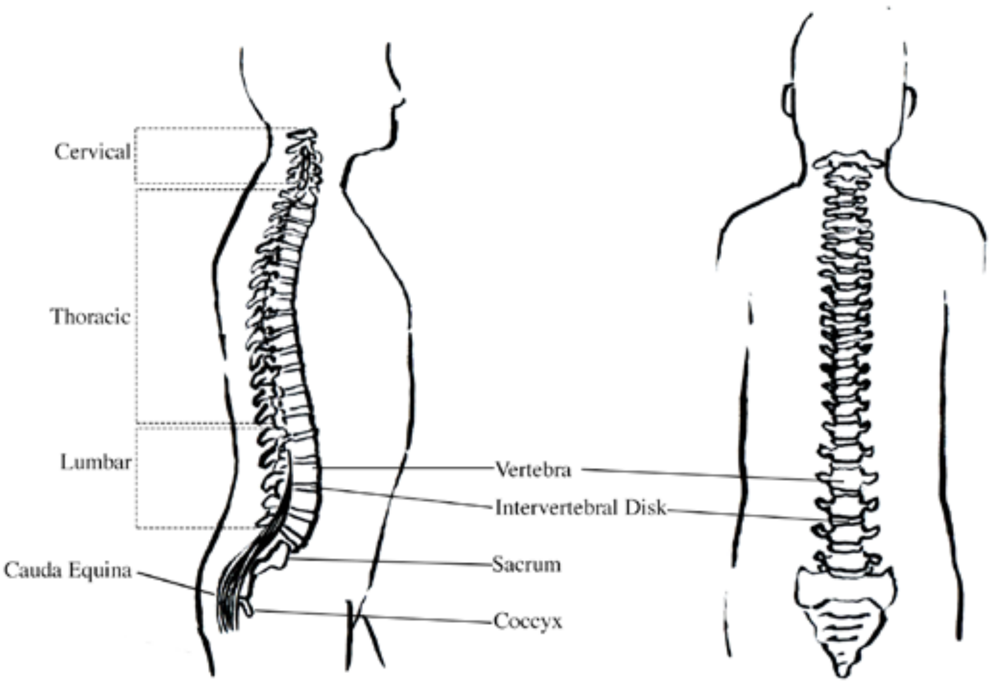

Figure 2. The normal, balanced vertebral column is also straight (has no rotation between the individual vertebrae) in erect position, coronal view. In the sagittal view, the distinctive curves can be seen.

2.1.1. Cervical spine

The complex and functionally diverse clockwork of the cervical spine has enabled humankind to thrive in the early stages of life with better visibility, mobility and enabling a balanced upright posture. The unique structure supports the head and enables its rotational movements. Half of this movement comes from the atlas-axis (C1-C2) complex and the rest is distributed down to the cervical vertebras c3-c7. Normal range of motion of the cervical spine is flexion 80-90 degrees, extension 70 degrees, rotation up to 90 degrees to both sides and lateral flexion from 20-45 degrees on each side (Penning, 1978).

Bony and ligamentous structures make the stable construction of the atlanto-axial joint. Bony structures are the odontoid process and the anterior arch of C1 vertebra. The transverse ligaments hold the odontoid against the anterior arch of this C1 vertebra.

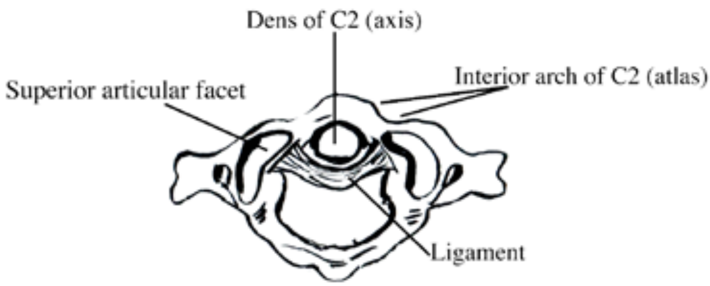

Figure 3. Atlas Superior View

The alar ligaments connect the odontoid to the occipital condyles. Other stabilizing ligaments are the apical ligament, which runs from the odontoid to the foramen magnum, and the cruciate ligament. (Sobotta Atlas of Human Anatomy, 1989)

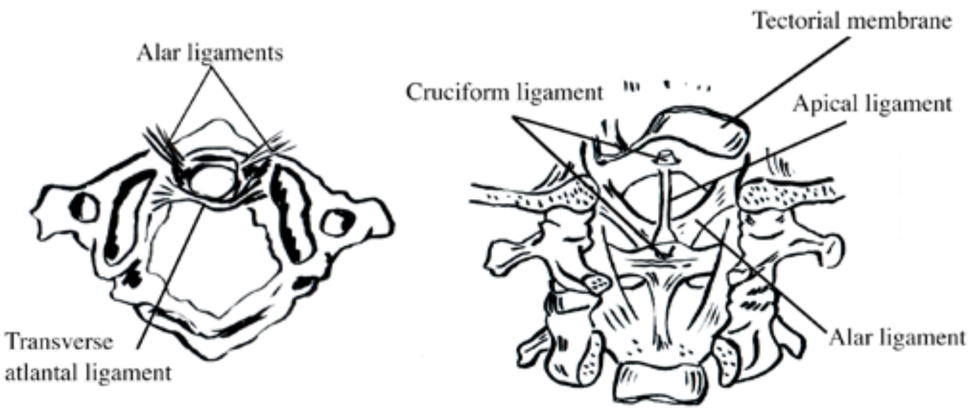

Figure 4. Ligaments of Atlas and 2nd Cervical Vertebrae

2.1.2. Thoracic Spine and Junction between the Thoracic Cage and Spine

Thoracic spine consists usually 12 vertebras. These join to each other and to the cervical and lumbar part of the spine. Each thoracic vertebra has bilateral costovertebral joint complex to the rib bones, which form the thoracic cage. This cage embeds vital elements of the human body and shields the basic elements of respiratory and circulatory system. The movement of the thoracic cage produces the respiratory negative and the excess pressures vital to gas exchange.

The thoracic spine is dominantly the center point of scoliosis. The respiratory function of the thoracic cage is threatened if this longest part of the spine becomes altered from its straight coronal posture (Pehrsson K et al., 1991).

2.1.3 Lumbar spine

The lumbar spine usually consists of five lumbar vertebras, which conjoins together the thoracic spine and the pelvis. The typical mobility of the lumbar lordosis is essential in maintaining our posture. Stiffness of the lumbar spine increases during adolescent, at the very time point when scoliosis deformation process is at its worst.

2.1.4. The Pedicle

The pedicle is an element of the vertebra with a special relevance to surgery. With the triumph of the pedicle screw technique fixation, the knowledge on pedicle anatomy has become increasingly important. In the cervical spine, the pedicles are shorter and are bordered anteriorly by the vertebral artery canal. In relation to the rest of the spine the cervical pedicles have a small diameter. The pedicle transverse width increases when descending the spine. An exception to this rule is the upper thoracic spine, where the transverse decreases until vertebra T5. The sagittal pedicle width decreases in the lumbar spine, being progressively increasing in the lower thoracic spine (Figure 5 a,b).

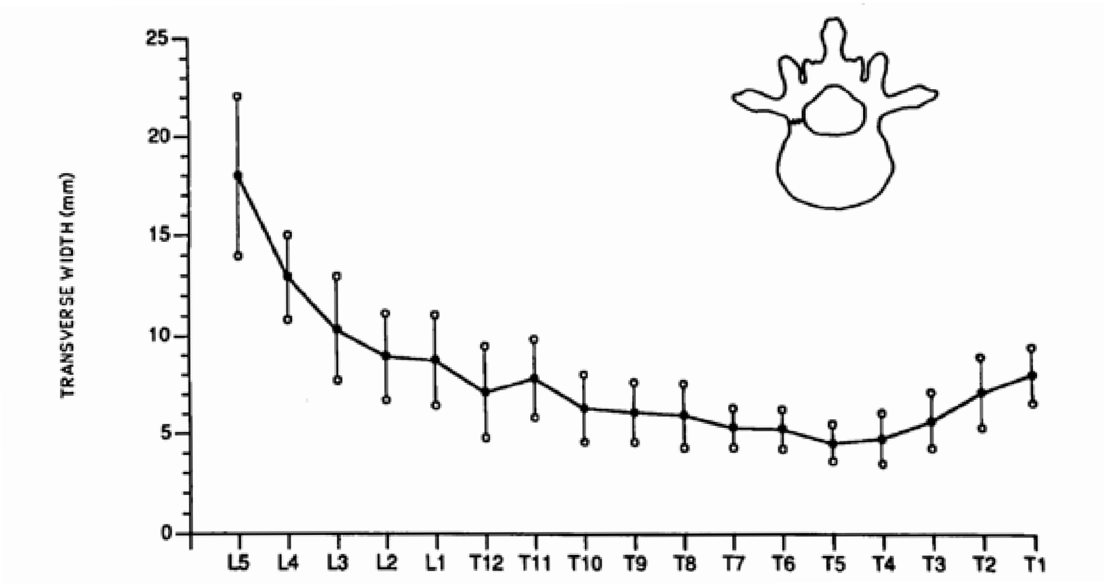

Figure 5a. Transverse and sagittal widths of the pedicles (Zindrick et.al. 1987)

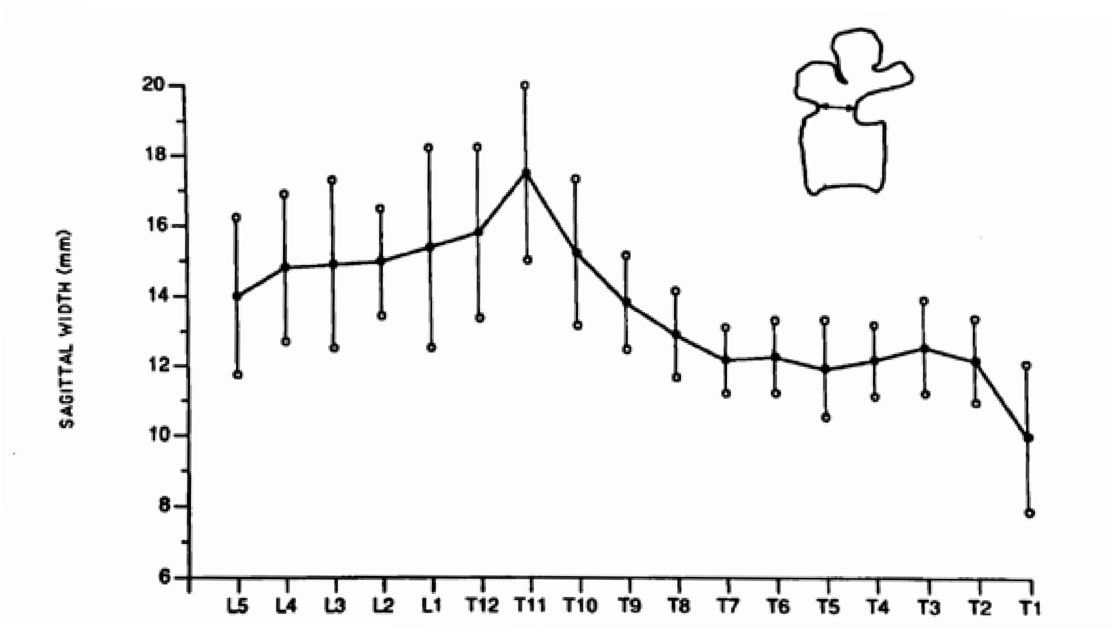

Figure 5b. Transverse and sagittal widths of the pedicles (Zindrick et.al. 1987)

2.2. Development and growth of the spine

2.2.1. The Atlas

The first vertebrae atlas is formed from three ossification centers.

- Anterior arch
- Two neural arches, which surround the anterior arch and fuse later in life to form the posterior arch.

These structures appear radiographically after the first year of age. Primary ossification centers at birth and secondary after birth. This normal ossification pattern has variabilities. Only one fifth of the newborn have ossification in the anterior arch and becomes visible as an ossification center by 1 year of age (Junewick J et al. 2011) (Figure 6).

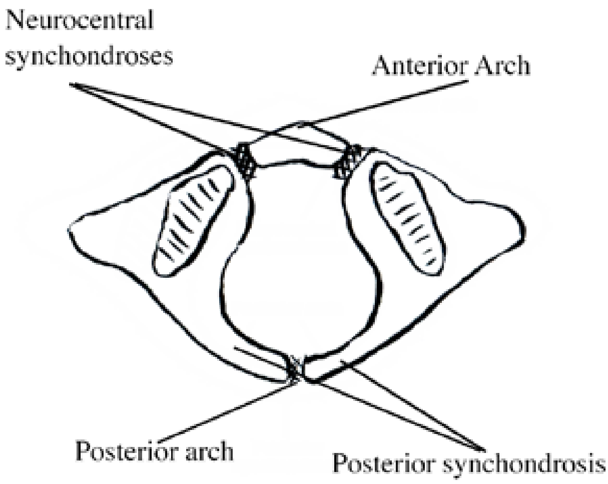

Figure 6. Synchondrosis of Atlas

The neurocentral synchondroses fuse between 5 and 8 years of age, and the posterior synchondrosis fuses by 5 years of age. The fusion of the posterior arches is formed after the 3rd year of age. The fusion of the lateral masses to the body happens after the 7th year at the neurocentral synchondroses. Due to this adjacent fusion we can detect that the internal diameter is at its completion at the age of seven. External growth of the atlas continues after this period. (Lustrin et.al. 2003)

2.2.2. The Axis

Second cervical vertebrae the axis develops from five ossification centers, the body, lateral masses comprised from two ossification centers, and part of the dens (odontoid process). By age of six, most children have closed dentocentral synchondrosis. The tip of dens fuses after the ossification of the root of the dens. This happens usually when child is 12 years old.

2.2.3. Subaxial Cervical Spine

The segments from C3 to C7 are created from center and two posterior arches. These arches evolve from mesenchymal tissue migrating around the neural tube. Superior and inferior ring apophysis ossify during late childhood. These fuse to the vertebral body by the age of 25. Other ossification centers – transverse and spinosus processes – fuse by three years of age.

2.2.4. Thoracic spine

Two thirds of the final sitting height is achieved by the age of 5 years. The growth velocity of the T1 to L5 segment is greatest from birth to age 5 years with marked deceleration between ages 5 and 10 years. Growth velocity increases again at age 10 years and after but does not equal the velocity occurring the first 5 years (Scott Y et al.,2016). Thoracic volume is approximately 6% of adult volume at birth, reaching roughly 30% of adult volume by age 5 years and 50% by age 10 years. (Lloyd-Roberts G. et al., 1965).

The significant increase in the growth of the spine and chest is associated with the synchronous growth of the lung parenchyma.

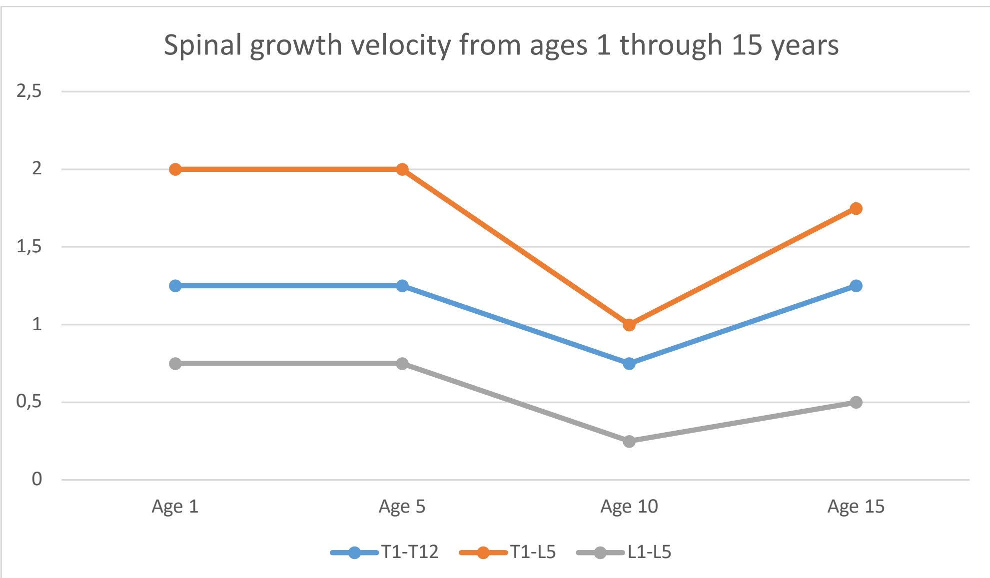

Figure 7. Growth of the spine before age 15 years (Redrawn from the table Dimeglio A, 1993).

2.3. Cervical Instability

Cervical instability is clinically and genetically heterogeneous group of disorders characterized by disturbances in the formation and/or growth of bone – skeletal dysplasias.

Syndrome	**Characteristic spinal abnormalities**
Larsen Syndrome	Cervical kyphosis and instability
Diastrophic Dysplasia	Midcervical kyphosis Cervical spina bifida Scoliosis, and/or exaggerated lumbar lordosis
Down Syndrome	Cervical instability
*22q11.2 Deletion Syndrome (*DiGeorge, CHARGE)	Cervical spine abnormalities, increased segmental motion
Pseudoachondroplasia	Os odontoideum Odontoid hypoplasia Instability at C1 to C2
Spondyloepiphyseal Dysplasia Congenita (SEDC)	Atlantoaxial instability (40%) related to odontoid hypoplasia or os odontoideum, along with ligament laxity
Mucopolysaccharidoses (MPS)	Atlantoaxial instability from odontoid hypoplasia
Kniest Dysplasia	Atlantoaxial instability

Table 1. Most common syndromes resulting in cervical instability (Modified from McKay et al 2012)

Clinical signs of instability may occur gradually and can be difficult to note. Neck pain can only be subtle and more severe symptoms, such as myelopathy, syncope, or radiculopathy, may be the final signs. Of the various skeletal dysplasias, the spondyloepiphyseal dysplasia (SED), spondyloepimetaphyseal dysplasia, pseudoachondroplasia, Kniest syndrome, and chondrodysplasia punctata are particularly susceptible to cervical instability, although many patients are initially asymptomatic. The instability of the upper cervical spine may progress to subluxation and dislocation and subsequently lead to cervical myelopathy, quadriparesis, and possible death (Skeletal Dysplasia Group, 1989).

Finding	**Typical syndrome**	**Radiographic examinations**	**Typical radiographic findings**
C0/C1 instability	Osteogenesis imperfect	Flexion-extension series of x-rays and MRI, CT scan	Joint laxity
C1/C2 instability	SED	Flexion-extension series of x-rays and MRI	C1 and dens gap exposed more than 5 mm in flexion-extension
subaxial instability	Diastrophic dysplasia, Larsen syndrome	Radiographs, Flexion-extension series of x-rays	Sagittal balance kyphotic due to hypoplasia and laxity

Table 2. Evaluation of cervical instability according to syndrome, radiograpahic examinations and typical findings

2.4. Scoliosis

Scoliosis refers to a complex deformity of the spine in all three planes. Initially, it was characterized as a medical condition in which a normally straight spine has a sideways curve exceeding 10 degrees observed through posterioanterior direct radiography (Cobb 1948). For a long time, the severity of scoliosis was assessed merely by the degree of the Cobb angle in coronal view radiographs (Cobb 1948). However, the deformity is seen as a significant rotation of the spine in forward bending often with unleveled shoulders and an asymmetrical waist. In radiographic images the curve is often "S"- or "C"-shaped. Today, the severity of the scoliosis deformity is estimated also using sagittal views and the alterations are compared to the normal spine.

Scoliosis is classified by its etiology into idiopathic (most common), neuromuscular, and congenital (Blevins K. et.al. 2018). The onset of the condition varies, and it can present itself at early-age (early-onset scoliosis), before adolescence, at adolescence, or in the adulthood (adult onset scoliosis). Despite the fact that numerous potential etiologies for idiopathic scoliosis have been proposed, the primary etiology remains unknown (Dayer R et al. 2013, Kikanloo S et al.2019).

Scoliosis	**Onset**	**Etiology**
Early onset scoliosis	< 10 years of age	Unknown
Neuromuscular scoliosis	From birth	Muscle and neurological deficit
Adolescent idiopathic scoliosis	10 years or later	Unknown
Congenital scoliosis	From birth	Congenital vertebral anomalies
Syndromic	Varies	Genetic inheritance

Table 3. Different types of scoliosis

2.4.1. Early-Onset Scoliosis

Early-onset scoliosis (EOS) is defined as curvature of the spine exceeding 10° in children. The onset of the scoliosis is prior to 10 years of age. Children with EOS are at tangible risk for impaired pulmonary function because of the high risk of progressive spinal deformity and thoracic constraints during a critical time of lung development (Scott Y et al., 2016). The number of alveoli increases more than 10-fold between birth and adulthood, primarily during the first 8 years of life. In addition, the number of respiratory branches increases from 21 at age 3 months to 23 at age 8 years (Dunhill M. 1962; Emery J et al. 1960). This leads children younger than 5 years of age particularly vulnerable to dangers of restricted growth due to EOS. Case reports from autopsies of children dying of EOS have shown restricted growth-induced abnormalities in both alveolar and pulmonary structure (Lewis, CS et.al., 1952), as well as pulmonary vascular remodelation associated with pulmonary hypertension (Davies G. et al. 1971).

Patients with no other obvious associated abnormalities are considered to have an early onset idiopathic scoliosis (EOS). The other subtypes EOS are congenital or structural, neuromuscular (e.g. cerebral palsy, myelomeningocele, muscular dystrophies), and syndromic (e.g. neurofibromatosis) (Williams et al. 2014).

2.4.2. Adolescent idiopathic scoliosis

Adolescent idiopathic scoliosis (AIS) is the most common spinal deformity found in humans. These consists nearly 80% of patients with structural scoliosis. The diagnostic test for scoliosis is so called Adams forward bend test, which is used in school screening (Kotwicki T et al. 2013) (Figure 8). Adolescent idiopathic scoliosis is a structural, lateral, rotated over 10 degree curvature of the spine that is found in normal children in the age of 10 or more. The diagnosis is made by posterior - anterior (pa) standing radiograph determining the coronal balance of the spine. Cobb angle is measured from the most tilted vertebras on the coronal view. The diagnosis is then found by excluding factors also causing scoliosis, such as leg length discrepancy , vertebral malformation, neuromuscular disorder, and syndromic disorders.

The progression of scoliosis is slow in childhood and escalates during the rapid growth in adolescents. The natural history of AIS depends on the severity of the curve (Weinstein et al. 1981). This means that, if scoliosis is diagnosed, a regular follow-up is recommended (Deurloo et al. 2015, Skalli et al. 2017).

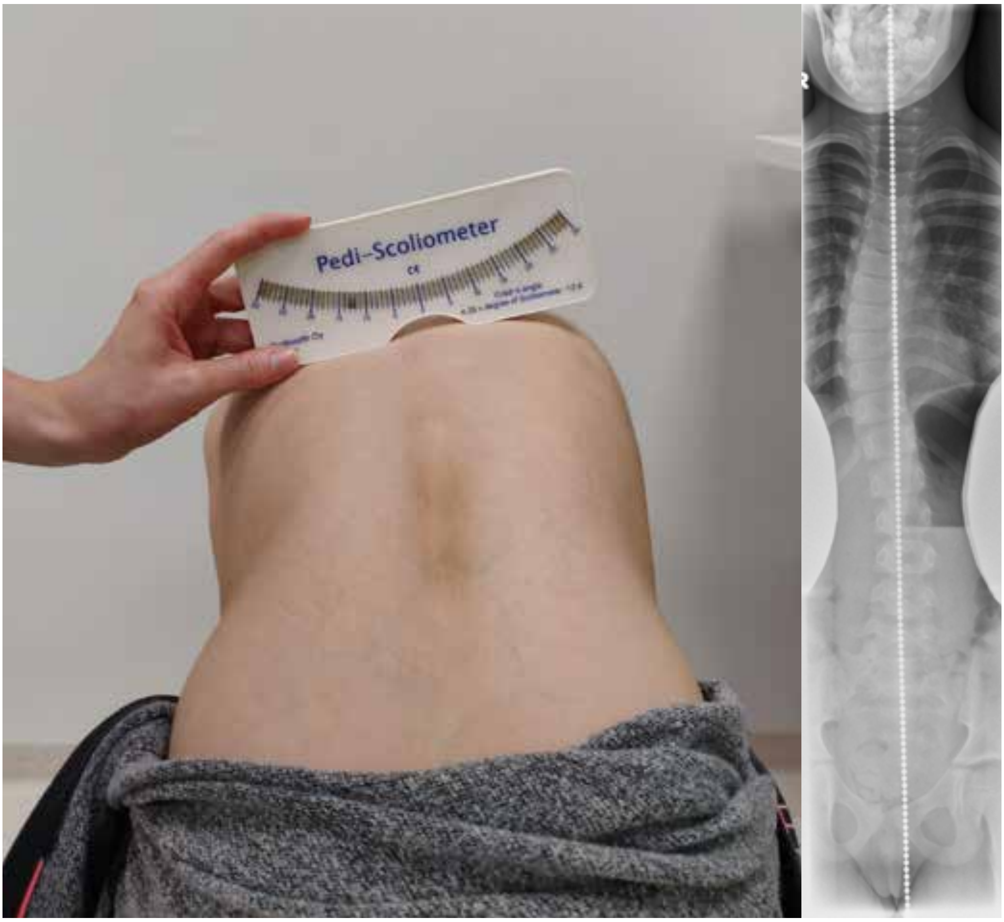

Figure 8. Determination of rib hump (left) and radiograph showing a mild scoliosis (right).

2.4.2.1. Epidemiology and Etiology of idiopathic scoliosis

The incidence of idiopathic scoliosis in radiographic studies, in a scholar population, ranges from 0.3 % to 15.3 %. When curves are analyzed according to their severity, the prevalence estimates change (Table 4) (Wajchenberg et al. 2016).

Prevalence of idiopathic scoliosis	
General prevalence of AIS	0.3–15.3 %
Curve > 10°	1.5–3.0 %
Curve > 20°	0.3–0.5 %
Curve > 30°	0.2–0.3 %

Table 4. Prevalence of idiopathic scoliosis according to curve severity

Etiology of AIS is believed to be multifactorial (Wajchenberg et al. 2016, Kikanloo S et al. 2019). According to one hypothesis, the anterior column of the spinal complex grows more rapidly than other parts. Combined with gravity and decreased mechanical stiffness of the intervertebral disks, this may lead to a rogue growth phenomenon seen in the coronal plane along with a rotational deformity (Drevelle X et al. 2010). Other proposed etiological theories are listed in table 5.

Hypothesis	**Author**
Relative anterior spinal overgrowth	Drevelle X et.al. 2010
Leptin dysfunction	Tam E et.al. 2014
Anatomical alterations of neural tissue	Grimes DT et.al. 2016
Melatonin deficit	Dubousset et al 1983; Wang et.al. 2014
Lesion in the anterior horn of the spinal cord	Spencer GS et al. 1976
Aymmetrical limbs and trunk growth	Wajchenberg,M et.al.,2016
Congenital myopathy	Wajchenberg,M et.al.,2015

Table 5. Studied theories related to AIS etiology.

2.4.2.2. Classification of Idiopathic scoliosis

Various classifications for different scoliosis types have been described. King et al. measured scoliotic deformities on coronal radiographs and described five thoracic curve types (King et. al. 1983). This classification did not include thoracolumbar, lumbar, or double or triple major curves. Lenke et al. published 18 years later a validated classification (Lenke et. al. 2001) which has gained popularity in the clinical use. This classification system has three components:

- curve type (1 through 6)
- lumbar spine modifier (A, B, or C)
- sagittal thoracic modifier (−, N, or +)

The classification is based on six curve types (Table 6). The lumbar spine modifier is based on the relationship of the center sacral vertical line to the apex of the lumbar curve. The sagittal thoracic modifier is based on the sagittal curve measurement from the fifth to the twelfth thoracic level (Lenke L et. al. 2001)

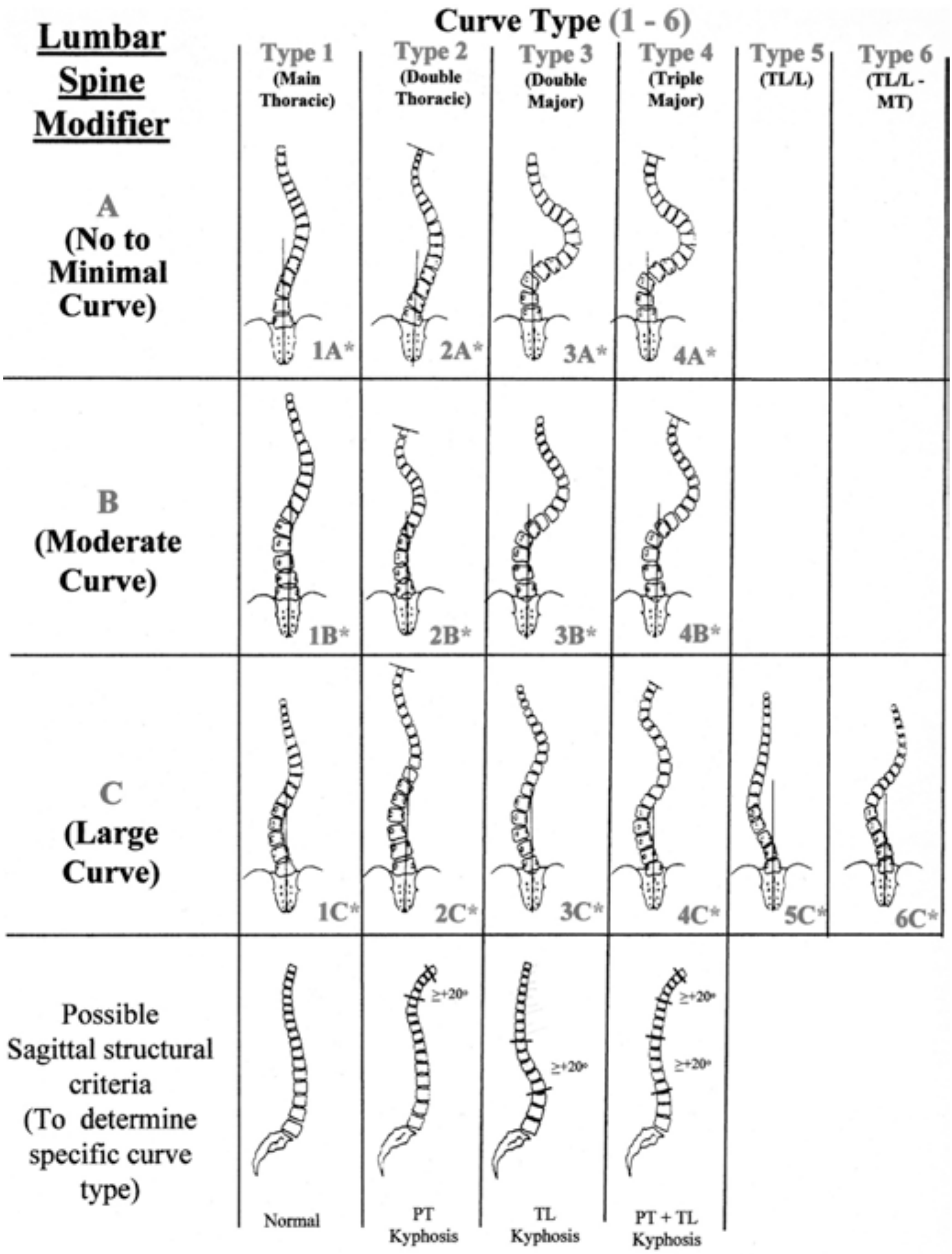

Table 6. Lenke classification of scoliosis (Lenke L et al 2001).

2.5. Severe Scoliosis

Untreated severe scoliosis of 70 degrees or more is associated with increased mortality as compared with normal population (Pehrsson et al. 1992) Most patients with scoliosis of 60 degrees or more present with major spinal deformity, restrictive lung disease and if left untreated rapid progression of the deformity (Newton PO et al. 2005 , Watanabe K et al. 2008, Kim YJ et al. 2005, Soliman H 2018)

Surgical options to correct severe spinal deformities include following procedures:

- anterior release and posterior instrumentation,
- pre- and perioperative halo-gravity traction, and
- spinal osteotomies such as vertebral column resection (VCR)

(Watanabe K et al. 2008, Dobbs MB et al. 2006 , Kuklo TR et al. 2005, Helenius I, et al. 2012, Hamzaoglu A et al. 2008, Koller H et al. 2012, Bradford DS et al. 1997 , Suk SI et al. 2002, 2005, 2008, Lenke LG et al. 2009, Sponseller PD et al. 2008 , Ledonio CGT et al. 2011, Phillips JH et al. 2013).

2.6. Neuromuscular scoliosis

Neuromuscular scoliosis (NMS) is a diverse group of diseases with a common denominator of progressive scoliosis driven by abnormalities in the neuromuscular system. This heterogenous group consists of patients with a traumatic spinal injury, patients with one or several neurological or muscular diseases such as cerebral palsy, postmeningitis encephalopathy, posttraumatic encephalopathy, poliomyelitis, myelomeningocele, spinal muscle dystrophy, muscular dystrophies, and myopathies. Apart from the scoliosis, these patients also have a vast variety of other musculoskeletal problems, such as dislocations of the hip joint and severe joint contractures with malalignment of the joints of the lower extremities. (Vialle R et al., 2013, Mary P et al. 2018).

2.6.1. Epidemiology and etiology of Neuromuscular scoliosis

The incidence of scoliosis in patients with neuromuscular conditions may range from 25% to 90% (Sarwark J et al., 2007). Unlike the idiopathic type, neuromuscular scoliosis tends to progress even after skeletal maturity. In a prospective study among institutionalized patients, Madigan found that the severity and incidence of scoliosis increases with the degree of mental retardation and decreased functional status in institutionalized cerebral palsy population. The types of cerebral palsy in the group consisted of 75% spastic, 8% dyskinetic, 4% ataxic, 8% mixed, and 5% undefined. Scoliosis was most common in the spastic group with the highest incidence in the spastic quadriplegics. The incidence directly paralleled the severity of the neurologic deficit but also appeared to be aggravated by the effects of gravity when the individuals were artificially placed in the sitting position. (Madigan R et al. 1981).

3. Treatment of scoliosis

3.1. Non-Operative Treatment

Non-operative treatment of scoliosis consists of observation, physical exercise, physiotherapy, electric stimulation, use of traction, and bracing (Nachemsson et al. 1995).

However, evidence on the efficacy of conservative treatment remains unproven (Negrini S et al. 2018). The only modality with high-quality evidence on benefit, as assessed by the progression of the severity and outcome of scoliosis measured by radiographs, is on bracing with rigid thoracolumbosacral orthosis (Weinstein et al. 2013, Negrini et al. 2018).

3.2. Operative treatment

3.2.1 First Techniques

Operative treatment for scoliosis has been performed for over a century. First spine instrumentations were set in the early 1920s. Before this era, the pioneers tried to resolve the scoliotic spine problem using strut graft splints to stop the deformative process. The pioneer of modern spinal surgery, Dr. Harrington, invented the Harrington rod (Harrington 1962) with the aim to straighten the scoliotic spine. In this system, hooks were attached to posterior spinal elements: facets, laminae and transverse processes. These pivot points then served as mounting points to distract the concave side. On the convex side compressive forces were introduced. Later, Eduard Luque developed sublaminar wires as a fixation method. This method is still used widely all over world in the treatment of neuromuscular patients (Luque 1982) (Figure 9).

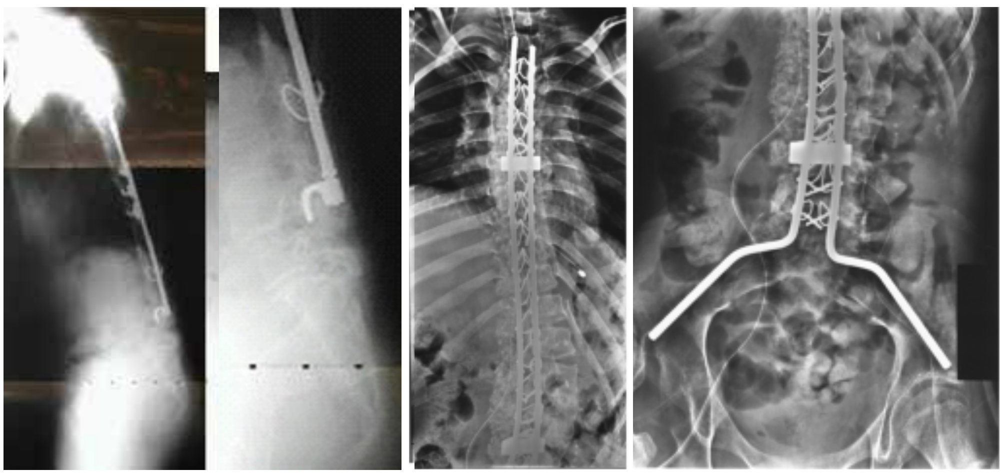

Figure 9. Harrington rod in place (left) and sublaminar wiring (right).

The next major step was the Cotrel Dubousset (CD) system named after the initials of its inventors Doctors Yves Cotrel and Jean Dubousset (Cotrel et al. 1988). This method attempted to control all three planes of deformity using a segmental placement of laminar hooks: coronal, sagittal and axial. Numerous publications have documented clear improvements in the correction of idiopathic scoliosis using this technique: Deformities of the rib were reduced, curve correction was in the range of 48% to 69%, and the sagittal alignment was restored literally for the first time in deformity spine surgery (Lenke et al.1995; Helenius et al. 2003). The flat back problems seen using the original Harrington rod technique were avoided when the fusion was lengthened to third and fourth lumbar vertebra. This was also crucial in order to preserve a natural lumbar lordosis.

3.2.2. Hybrid Technique

Hybrid technique, which combined the use of laminar hooks, sublaminar wires, and lumbar pedicle screws, were the next evolution in the surgical technique (Figure 10). In this technique, the lumbar part of the spine is fixed with pedicle screws, the upper thoracic part with laminar hooks, and midthoracic using a combination of concave wires and convex hooks. The fixation allows a substantial movement at the upper thorax and thus the correction is not rigid. On other hand learning curve is shorter and complications are not so devastating compared to total pedicle screw technique. As the technique leaves the spine flexible, the correction of the deformity was not as complete as with more modern techniques (Cheng et al. 2005). Introducing this technique to rigid deformity proved challenging, as it usually required vast releasing procedures prior to correction maneuvers.

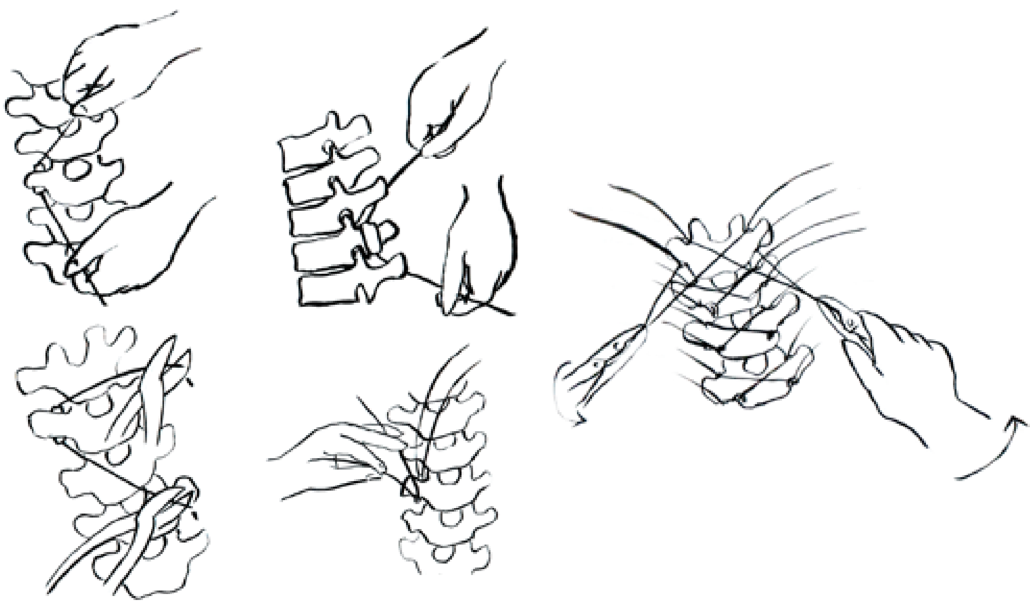

Figure 10. Sublaminar wiring technique.

3.2.3. Pedicle Screw Technique

Pedicle screws are the current mainstay in scoliosis surgery (Suk et al. Spine 1995, Kim YJ et al. 2004, 2006) (Figures 11a and 11b). In this technique, screws are inserted into vertebral pedicles and rods are hooked into screw heads to allow rigid fixation. Pedicle screw technique allows correction of the various, individual segmental deformities. One of the primary asserted benefits is the prevention of the flattening of the thoracic kyphosis.

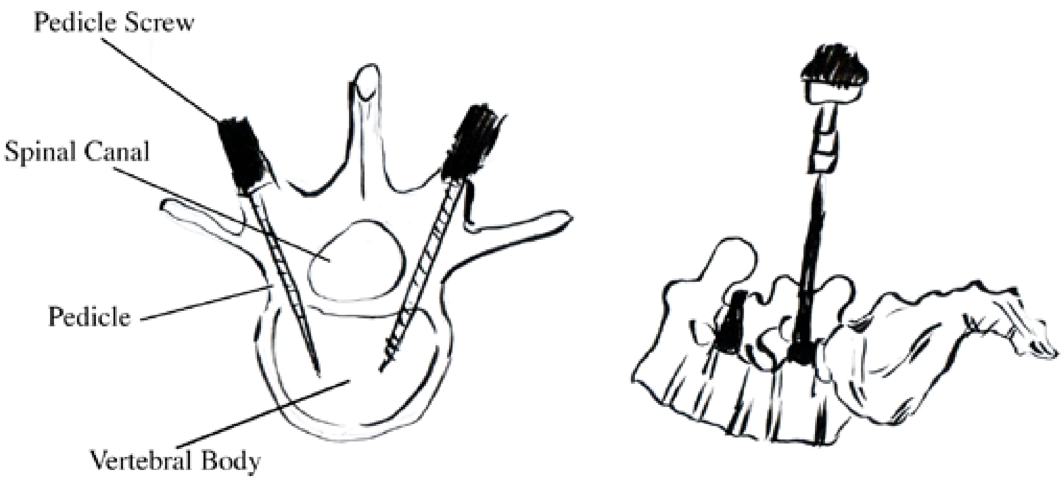

Figure 11a. Pedicle screw technique, inserting the screwsf

Figure 11b. Pedicle screw technique, correcting rods in place

3.2.4. Operative Management of NMS

The surgical techniques for NMS correction have gone through major change over the past decades. Before the introduction of the pedicle screws, a combined anterior/posterior approach was favoured. Anterior discectomy and release of the anterior longitudinal ligament together with posterior instrumentation provide excellent arthrodesis and flexibility for a rigid spinal deformity, while preventing the crankshaft phenomenon in skeletally immature patients and allowing for correction and maintenance of pelvic obliquity (Ferguson R et al., 1996). The crankshaft phenomenon, a progressive rotational and angular spinal deformity that can occur after posterior spinal surgery. This phenomenon can occur after posterior spinal surgery (Murphy R et al. 2017).

Posterior segmental instrumentation to treat NMS evolved from hybrid constructs with hooks, pedicle screws, and sublaminar wires accompanied with anterior release procedure to posterior only operation solely to the use of pedicle screws. This posterior-only procedure quickly gained popularity, as it was less traumatic and could be performed as a one-day surgery.

3.3. Skeletal Dysplasias and Cervical Instability

The skeletal dysplasias are a clinically and genetically heterogeneous group of disorders characterized by disturbances in the formation and/or growth of bone (Table 7.) Numerous dysplasias are associated with cervical instability.

Surgical treatment is complicated by petite and fragile bony spinal elements with low bone formation rate. In addition, most studies include both pediatric and adult patients with upper and lower cervical spine fusions as well as non-instrumented and instrumented spinal fusions. None of these studies have reported quality of life outcomes. Outcome evaluation is complicated, since not only spine disorders, but also other orthopaedic problems, such as small stature, tethered spinal cord and early joint degeneration may affect outcomes (Lastikka M et al. 2017).

Syndromes
Spondyloepiphyseal dysplasia
Spondyloepimetaphyseal dysplasia
Pseudoachondroplasia
Kniest syndrome
Chondrodysplasia punctate
Diastrophic dysplasia

Table 7. Different skeletal dysplasias with cervical instability

3.3.1. Cervical Spine Instrumentation, posterior techniques

Atlantoaxial instability is a particularly dangerous situation. It generates from many reasons e.g. trauma, congenital malformation and tumor. Posterior atlantoaxial fixation techniques are classified into six main categories (Table 8.)

Technique		
Wiring techniques	Gallie technique	Sublaminar C1 wire is looped underneath the C2 spinous process with an interposed iliac crest bone graft.
	Brooks Jenkins technique	4 monofilament 20-gauge sublaminar C1 and C2 wires compress 2 separate wedge shaped iliac crest bone grafts.
Interlaminar clamp fixation		
Atlantoaxial transarticular screws	Screw fixation	
Screw-plate system fixation	Pedicle screws and lateral screws, plate	
Screw-rod system fixation	Pedicle screws and lateral screws, rods	
Hook-screw system fixation techniques	Screws, hooks	

Table 8. Posterior atlantoaxial fixation techniques. (Da-Geng H, 2015)

3.3.2. Wiring techniques

The first generally accepted wire fixation system used clinically was the Gallie technique. In this technique a 20-gauge sublaminar wire is looped from the posterior part of the first cervical vertebrae (C1) and re-looped underneath the second cervical vertebrae (C2) spinous process with an interposed iliac crest bone graft. (Figure 12. Posterior techniques A and B). (Papagelopoulos J et al. 2007)

Another widely used fixation technique to fuse C1 and C2 is the Brooks-Jenkins technique. In this method 4 monofilament 20-gauge sublaminar wires compress C1 and C2 two separate wedge shaped iliac crest bone grafts. (Figure 12 Posterior technique C) Both Brooks-Jenkins and Gallie fixations alone gives a modest result when used for atlantoaxial arthrodesis. Both techniques have relatively high failure rate when used alone. (Papagelopoulos J et al. 2007)

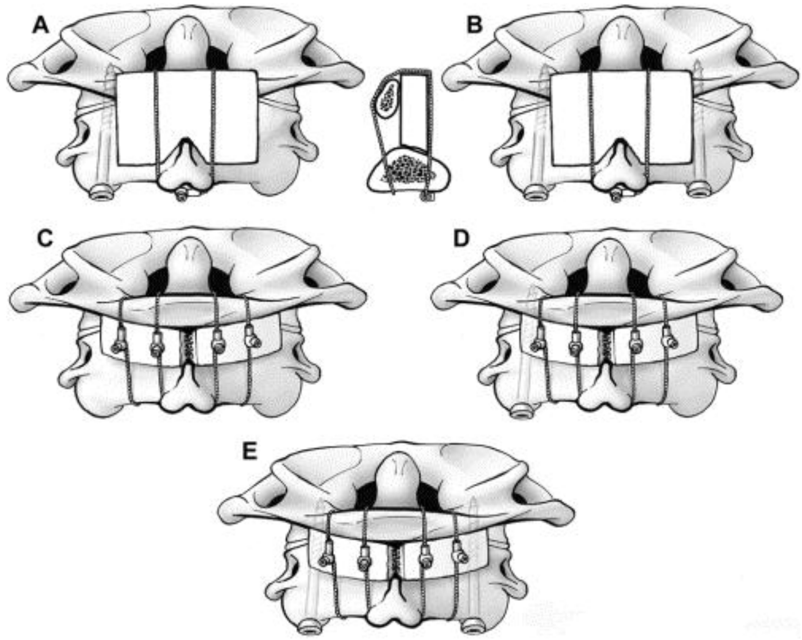

Figure 12. Posterior Techniques (Papagelopoulos J et al. 2007)

3.3.3. Screw techniques

Transarticular atlantoaxial screw fixation method was first reported by Jeanneret and Magerl in 1992 for C1–C2 stabilization. In this technique two transarticular screws are inserted into the bilateral atlantoaxial lateral joints to immobilize C1 and C2. (B. Jeanneret and F. Magerl, 1992)

This method is also commonly used in atlantoaxial immobilization especially when the C1 lamina is absent (Da-Geng H, 2015).

In in vitro studies the stability of the two wiring techniques (Gallie and Brooks Jenkins) were proven to be significantly lesser compared to techniques where transarticular screw fixation was combined with sublaminar fixations. The cable and bone graft with two screws provided the most stabilization in terms of the amount of translation allowed (Figure 12. Posterior techniques D and E) (Naderi S,1998).

3.3.3.1. Pedicle Screw Technique

Evolution in thoracic pedicle screw technique enhanced also the cervical instability surgery. The first evolution was the C1 lateral mass screw techniques in 1994 (Goel et al. 1994). Harms and Melcher modified and promoted it in 2001. In this widely used Harms technique, the entry point is the middle of the junction of the C1 posterior arch and the midpoint of the posteroinferior portion of the C1 lateral mass. (Figure 13. Da-Geng H, 2015).

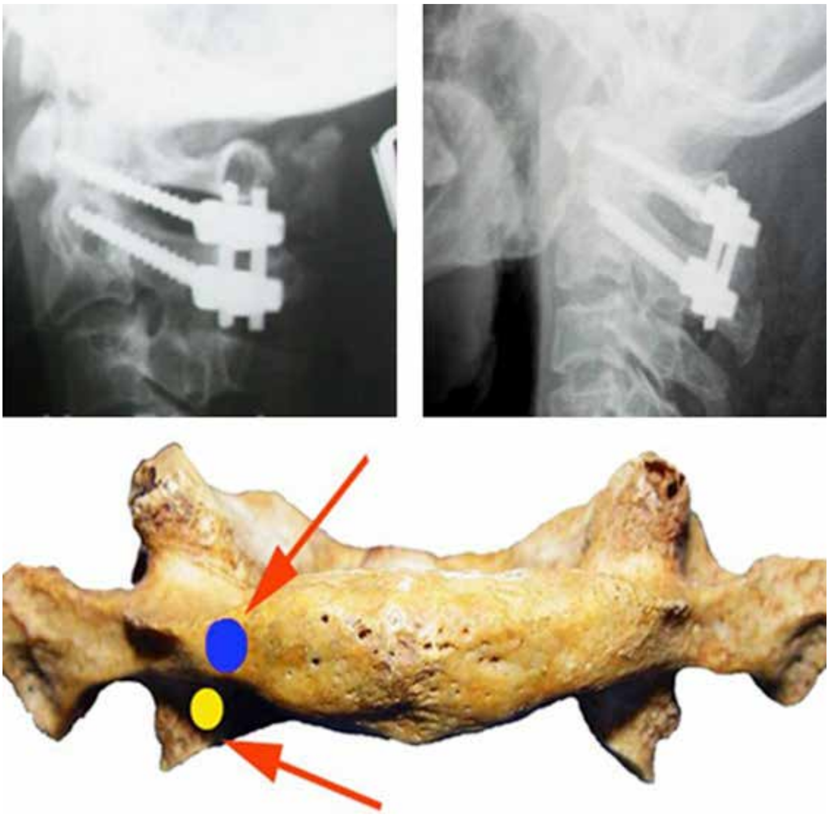

Figure 13. Harms technique (top left) and Pedicle Screw technique (top right), entry points C1 pedicle screw blue and C1 lateral mass screw yellow dot by Da-Geng H et al. 2015.

C1 pedicle screw fixation was first reported by Resnick and Benzel in 2002. In this technique, the pedicle screw is inserted to the C1 lateral mass via the posterior arch.
C2 pedicle screw fixation was also first described by Goel and Laheri, and later popularized by Harms and Melcher. The entry point is midway between the superior and inferior articular processes. The superior stabilization is achieved with rods attached to pedicle screws.

Different modifications have been introduced throughout decades. These are different combinations from wiring systems, hooks and screws. Also positioning of the screws have played a role in this development. The rapid development of the imaging technique has made the pedicle screw technique (screw-rod) safe and thus tempting. (Smith J et al., 2016, Jung-Woo H 2019).

Combination techniques:

- interlaminar clamp fixation
- screw-plate fixation
- screw-rod fixation
- hook-screw fixation techniques

4. Aims of the Study

1. To assess whether *en bloc* vertebral column derotation provides an efficient correction of thoracic rib hump as compared with no derotation in adolescents with an idiopathic scoliosis.

2. To compare the outcomes of hybrid versus total pedicle screw instrumentation in children undergoing surgery for neuromuscular scoliosis

3. To compare the hybrid versus total pedicle screw instrumentation on the morbidity and radiographic outcomes in patients with severe scoliosis of 90° or more

4. To study the outcome of upper cervical spine fusion in children with skeletal dysplasia.

5. Materials, methods and patients

5.1. Studies I-III

Studies I-II were all prospective follow-ups comparing two different treatment strategies in patients with scoliosis using two matched cohort design (Table 9). Study III was a retrospective study of prospectively collected data using two consecutive patient cohorts.

The designs of the studies I-III are summarised according to PICO(T) criteria (Schardt, C. et al., 2007) (Table 9 and 10). **PICO** (T) elements include: **P**roblem/**P**atient/**P**opulation, **I**ntervention/**I**ndicator, **C**omparison, **O**utcome, and **T**ime element (optional) or **T**ype of Study.

	Study I		**Study II**		**Study III**	
Patient/**P**opulation	Thoracis idiopathic scoliosis		Neuromuscular scoliosis		Severe scoliosis	
Intervention/**C**omparator	*En bloc*-DVR	Non-DVR	Hybrid	Total pedicle screw	Hybrid	Total pedicle screw
- Surgery performed (years)	2007-2008	2008-2009	2003-2006	2006-2009	2003-2006	2006-2011
- Number of patients	48	24	33	33	15	17
- Age (years), Mean (range/SD)	15.1 (10.5-18.0)	13.7 (9.0-17.5)	15.8 (3.0)	14.7 (2.5)	15.9 (3.0)	14.8 (2.8)
- Sex (male/female)	12/36	2/22	15/18	15/18		
- Type of scoliosis						
o AIS	45	21			1	
o JIS	3	3				
o Neuromuscular			33	33	12	16
o CP					9	7
o Syndromic					3	6
o Myopathy						1
o Hereditary polyneuropathy						1
o Secondary scoliosis					2	1
Outcomes	Summarised in the Results section.					
Time (follow-up), years Mean (range)	2.0 (2.0-2.0)	2.0 (2.0-2.0)	2.8 (1.2)	2.8 (0.3)		

Table 9. Patient characteristics according to the PICO(T) criteria.

TIMEPOINT	PRIOR TO SURGERY	POST SURGERY	6 MONTHS	1 YEAR	2 YEARS
BASELINE CHARACTERISTICS	I,II,III				
CLINICAL					
Neurological examination of lower extremities	I,II,III	I,II,III	I,II,III	I,II,III	I,II,III
Adams test (Rib hump)	I,II,III		I,II,III		I,II,III
IMAGING					
Coronal balance	I,II,III	I,II,III	I,II,III		I,II,III
Sagittal balance	I,II,III	I,II,III	I,II,III		I,II,III
Bending radiographs	I				
Traction radiographs	II,III				
Health-related quality of life	I, II (partially)	I, II (partially)	I, II (partially)		I, II (partially)

Study I, Study II, Study III

Table 10. The schedule of follow-up assessments.

5.1.1. Clinical examination

Follow-up examinations were performed by one of two orthopaedic spine surgeons (I.H. or M.M.). The patients underwent a systematic physical examination preoperatively, before discharge, and at follow-up visits (Table 10), which included:

- coronal balance evaluation
- sagittal balance evaluation
- measurement of thoracic and lumbar rib hump measurement using a scoliometer, (Bunnel W 1984)
- Neurologic examination of the lower legs.

Rib hump measurement was not performed at the time of discharge, since we did not allow patients to perform a forward bending test immediately after surgery. Thoracic rib hump measurements were available preoperatively and at final follow-up in 21 (88%) and 39 (81%) of the N-DVR and DVR patients, respectively.

5.1.2. Radiographic evaluation

Standard standing posteroanterior and lateral radiographs were taken of the entire spine pre- and postoperatively, and at follow-up visits (Table 10). Radiographic follow-up rate was 100%. Based on patients' ability, either standing or sitting radiographs were taken in studies II and III.

Measured angles from radiographs with Cobb technique:

- Proximal thoracic
- Main thoracic
- Thoracolumbar or lumbar curves
- pelvic obliquity

Coronal balance was determined as the horizontal distance of the spinous process of C7 from the centre sacral line measured in millimetres. Sagittal balance was measured from the lateral projection with a similar method by dropping a vertical line from the middle of C7 vertebral body and measuring the horizontal distance of the uppermost portion of S1 vertebral body from this vertical line. Correction of spinal rotation postoperatively was analysed using the Upasani scoring method (Upasani V et.al. 2009) for the main thoracic curve (Study I).

At least two independent observers measured all radiographs. Three independent observers measured all radiographs in study II. Although the inter-observer reliability of these observers was not verified these observers were experienced in analysing radiographs. Spinal radiographs in case of difficult deformity were measured based on a consensus decision and in borderline cases, the milder option was chosen. Spinal bending radiographs were obtained preoperatively to identify structural curves. The proximal junctional kyphosis was evaluated (Study II) at final follow-up only. In Study II, sagittal balance was not evaluated radiographically, since most of the patients were non-ambulatory.

5.1.3. Health-related quality of life

The Scoliosis Research Society 24 (SRS-24) questionnaire (Haher TR, 1999) was mailed to the patients and answers verified during the follow-up visits. The 24 questions in the questionnaire give a maximum score of 120, indicating a highly satisfied and asymptomatic patient. Filling of SRS-24 questionnaire was performed at home either by the patient or by caregivers depending on the patient ability (Study II) and returned at the follow-up visits. In study II complete SRS-24 scores were available for 18 patients (55%) in the hybrid and in 23 (70%) in the TPS groups. The answers were checked during the physical examination. In studies III-IV, Health-related quality of life questionnaire was not implemented.

5.2. Patients

In study I, two matched cohorts were formed in order to minimize the compounding effects of age at surgery, sex, and primary diagnosis as reliably as possible. For every N-DVR patient (n = 24), a DVR group patient, who matched the best for age at surgery (± 1 yr), sex, thoracic rib hump size (± 2°), primary diagnosis (JIS or AIS), and curve type (Lenke classification), was selected from the rest of the original study population (n = 48). Two N-DVR group patients could not be matched sufficiently and they had to be excluded.

In study II two groups were matched for age at surgery (±1 year), gender, the size of the curve (±10°) and basic neurological condition. It was not possible to match four patients (males) in the TPS instrumentation group, thus 33 matched pairs were created (Table 9.).

Study III included a total of 32 consecutive patients. First 15 consecutive patients were operated using a Hybrid instrumentation and the following 17 patients using a Pedicle Screw instrumentation.

5.3. Study Design

The study design was a retrospective study of prospectively collected data using two consecutive patient cohorts.
Examinations were performed by one of four orthopaedic spine surgeons

- before surgery
- on the day when the patient was discharged from the hospital
- six months
- two years after surgery

All patients were operated by at least two out of three orthopaedic spine surgeons, of which one was always the senior author. Pelvic fixation was performed when L5 tilt over S1 endplate was over 10 degrees. Standing or sitting posteroanterior and side radiographs of the whole spine (scoliosis) were taken preoperatively, immediately after surgery on table and during ward period as well as at six, and twenty-four months. Two independent observers measured all radiographs and the mean value was determined. Spinal radiographs in case of difficult deformity were measured based on a consensus decision and in borderline cases, the milder option was chosen. Standard preoperative imaging included anteroposterior spinal radiograph under traction and a full medical evaluation by a consultant paediatrician. Also renal and cardiovascular systems were investigated using ultrasound for associated anomalies. Mortality data was collected on all patients from our National Official Cause of Death statistics. Data on complications was recorded in a prospective manner. The study was carried out from August 2003 to February 2013.

5.4. Operative techniques

All patients were operated prone and posterior elements of the spine were exposed carefully with electrocautery. When pedicle screws were inserted it was done with the freehand technique on the basis of posterior bony elements according to Kim (Kim et al, 2004). In Study I fourteen (58%) patients without and 34 (71%) patients with DVR underwent Ponte procedure. Ponte procedure was performed in Study II to 5 (33%) patients in the Hybrid and 16 (94%) patients in the Pedicle Screw group.

In study II anteroposterior surgery was performed in the hybrid instrumentation group when the thoracic curve magnitude exceeded 70 degrees, thoracolumbar curves 100 degrees or in the immature patient to prevent crankshaft. Anteroposterior surgery in the pedicle screw instrumentation group was performed in extreme curves of 100 degrees with less than 25% correction on traction films and in none for the prevention of crankshaft phenomenon.

Anteroposterior surgery:

- 12 (80%) patients of the Hybrid group
- 2 (12%) of the Pedicle Screw group

Anterior approach was thoracotomy for the lower thoracic spine and thoraco-abdominal for the Th12-L2 area.

Apical vertebral column resection (VCR) was performed for three patients in both groups. Patients in the Hybrid groups underwent VCR using combined anteroposterior approach and patients in the Pedicle Screw group using all posterior approach according to previously described techniques (Hamzaoglu A, 2008). All patients received morselized allogenic bone grafting with iliac fixation.

Hybrid instrumentation included:

- upper thoracic hook claw on both sides
- sublaminar wires on the concave side
- mid-thoracic hooks on the convex thoracic spine
- lumbar pedicle screws

Pedicle screws were inserted with the free hand technique according to Kim et al. 2004. Multi-axial reduction screws are used at the apical concave side. Iliac fixation was for six patients in the Hybrid and 14 in the Pedicle Screw group using long iliac screws and connectors (p=0.014).

Epidural bleeding is controlled using bipolar cauterization and use of hemostatic agents such as human thrombin with gelatine matrix (FloSeal, Baxter US, Deerfield, IL). In study II spinal deformity correction was obtained by double rod cantilever maneuver or concave rod derotation.

Spinal cord monitoring (MEP, SSEP, lumbar nerve root EMG) was performed in all of the operations.

5.5. Study IV

Patients

Seven children with upper cervical instability due to skeletal dysplasia underwent cervical spine stabilization with or without decompression in our hospitals (Table 13). Three had spondyloepiphyseal dysplasia with marked C1/C2 or C0/C2 instability, one had osteogenesis imperfecta with severe basilar invagination, one had chondrodysplasia punctata with mid cervical (C3-C5) instability and tetraparesis since birth, one patient diastrophic dysplasia with upper cervical kyphosis associated with medullary compression, and one C1/C2 instability with asymptomatic spinal cord compression due to metatropic dysplasia. The disability caused by the cervical spine disorder was evaluated by the Scoliosis Research Society SRS-24 questionnaire.

#	Fusion	Syndrome	Age	Method	Cause of instability
#1	C1-C2 fusion	Spondyloepiphyseal dysplasia	4	Screw fixation, Brooks-Jenkins lamina wire fixation	Atlantoaxial instability 8mm, hypoplastic dens
#2	C1-C2 fusion	Spondyloepiphyseal dysplasia	7	Unilateral screw fixation, Brooks- Jenkins lamina wire fixation	Hypoplastic C2 vertebra, 5 mm instability
#3	C1-C2 fusion	Spondyloepiphyseal dysplasia	5	C1 laminectomy and a C0-C2 spondylodesis using metal wires	
#4	C0-C2	Chondrodysplasia punctata with mild tetraparesis	5		
#5	C0-Th5	Osteogenesis imperfecta type III	7	C1 laminectomy was performed, with decompression of the foramen magnum with occipito-cervico-thoracic instrumentation from C0 to Th5 using occiput plates, cervical hooks, lateral mass screws and thoracic pedicle screws	Basilar invagination associated with foramen magnum stenosis, Chiari-I malformation and mild hydrocephalus
#6	C0-C4	Metatropic dysplasia	16	C0-C4 instrumented fusion	C0/C2 marked instability and cervical spinal cord compression
#7	C0-C7	Diastrophic dysplasia and tetraparesis	1	Circumferential cord decompression with anteroposterior cervical spine fusion from occiput to lower cervical spine	

Table 11. Study IV patients

5.6. Statistical Analysis (Studies I-IV)

Values are given as means, standard deviations (SD) or ranges. A two-tailed independent T test was used to calculate the level of significance for continuous variables and $\chi 2$-test for categorical variables. P-values equal to or below 0.05 were considered statistically significant.

5.7. Ethical Aspects (Studies I-IV)

We obtained permission to every study from the Ethics Committee of Helsinki University Hospital at the place of the study. All subjects gave Informed Consent to participate in the study.

6. Results

STUDY I

Clinical findings

Patients in the N-DVR group were significantly younger than patients in the DVR group at the time of surgery (mean 13.7 years vs. 15.1 years, p=0.0033) and there tended to be more girls in the N-DVR than in the DVR group (p=0.092). The mean (SD) final correction of thoracic rib hump was 40% (±31%) in the N-DVR and 44% (±26%) in the DVR groups (p=0.62) (Figure 14).

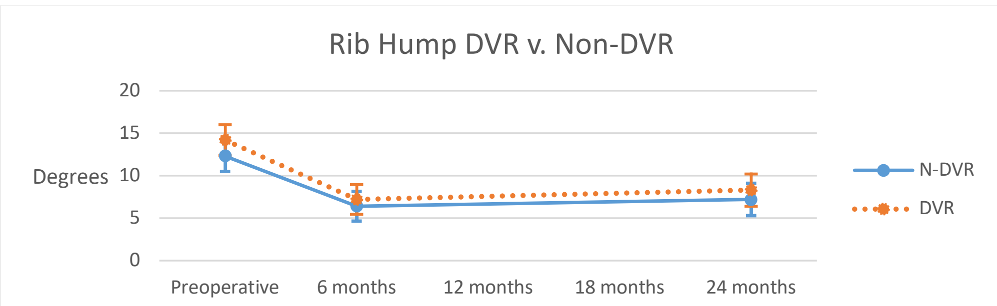

Figure 14. Rib hump correction in DVR (orange) and N-DVR (blue) groups.

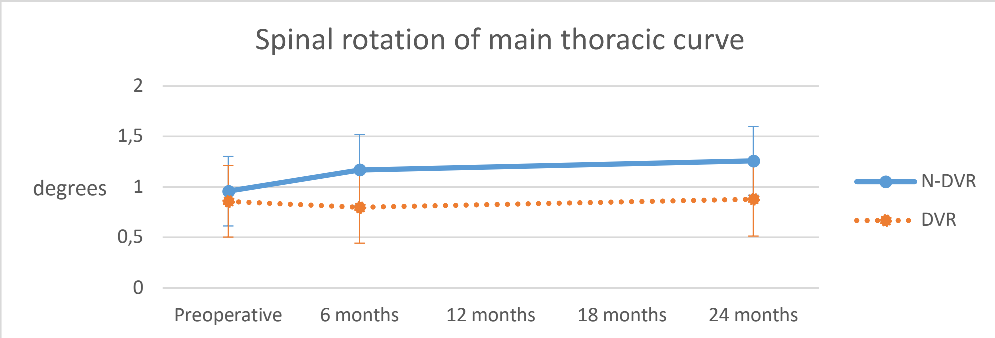

Figure 15. Spinal rotation correction in DVR (orange) and N-DVR (blue) groups.

Radiographic findings

Correction of spinal rotation as assessed by the Upasani score (Upasani V et.al. 2009) was significantly better in the DVR as compared with N-DVR group at 2-year follow-up (p=0.032). Correction of spinal rotation decreased significantly in the N-DVR group during the 2-year follow-up (p=0.0041), but not in the DVR group (Figure 15).

Radiographic results were otherwise similar between the two groups. (Figures 16-17).

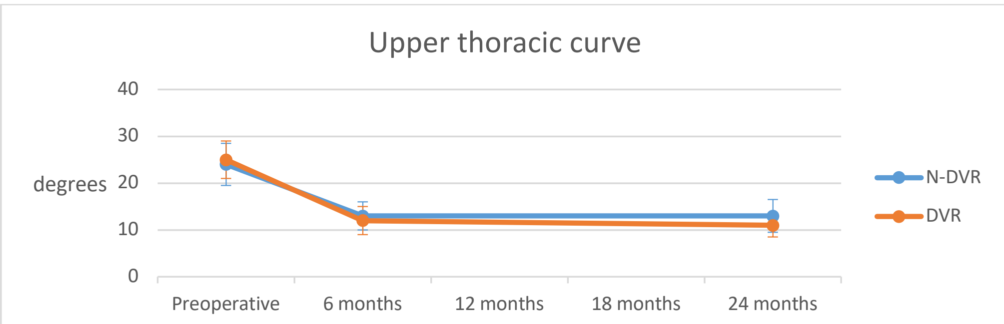

Figure 16. Upper thoracic curve

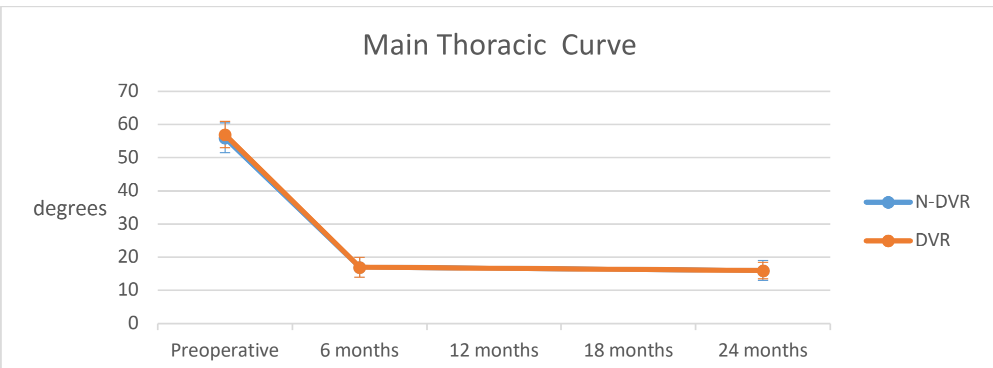

Figure 17. Main thoracic curve

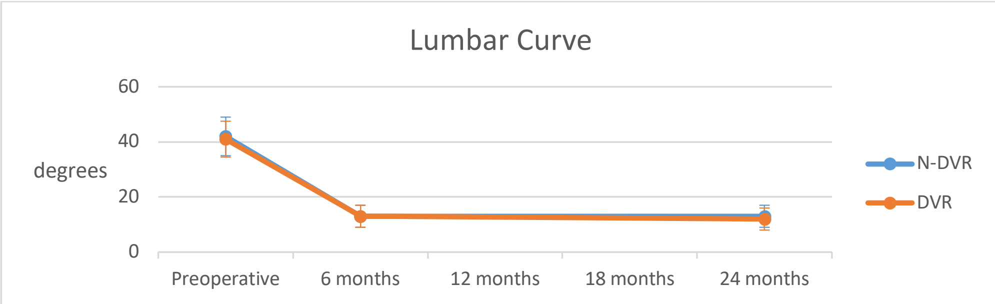

Figure 18. Lumbar curve

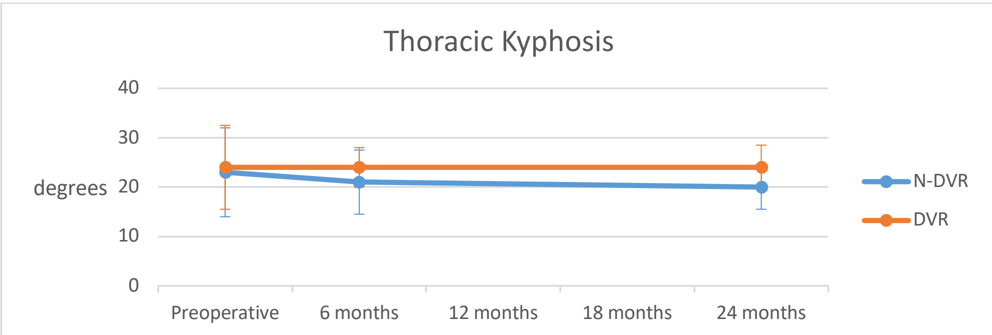

Figure 19. Thoracic curve

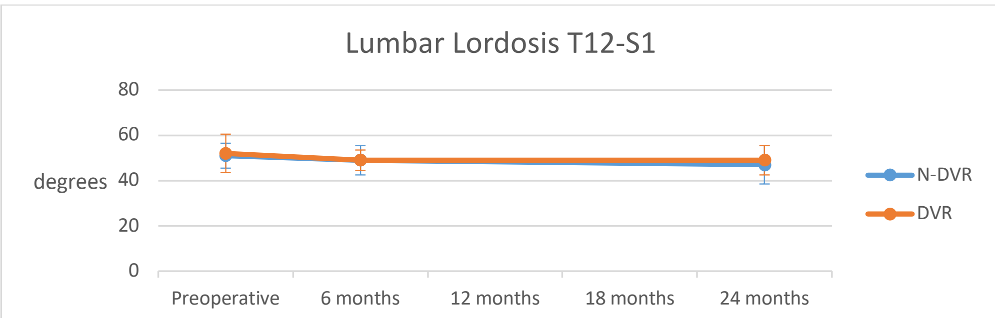

Figure 20. Lumbar Lordosis

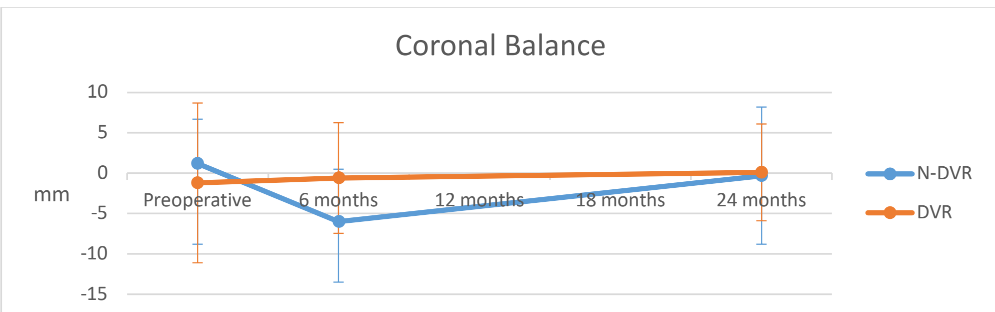

Figure 21. Coronal balance

Thoracic kyphosis tended to flatten in the N-DVR group, while no such change occurred in the DVR group (p=0.11 between groups at 2-year follow-up) (Figure 19). No difference in the mean thoracic kyphosis was noted in patients operated with 5.5 mm or 6.35 Ti Alloy rods (Figure 19). Coronal unbalance (>20mm) was found in three (13%) in the N-DVR and four (8%) patients in the DVR groups, respectively (p=0.57). Positive sagittal balance of 20mm or more was observed in seven (29%) and 11 (23%) of the study groups (p=0.56), but none of the patients had a sagittal vertical line in front of the midpoint of the femoral heads (Figure 21).

Health-related quality of life

The SRS-24 total score averaged at two-year follow-up:

- 100.4 (SD ±5.7) points in the N- DVR group
- 99.3 (SD ±9.0) in the DVR group

No significant differences existed in the seven main domains of SRS-24 between the study groups at two-year follow-up.

STUDY II

Clinical findings

The mean age at operation was 15.8 years (SD ± 2.99; range 9.1-19.6) in the hybrid group and 14.7 years (SD ± 2.50; range 7.0-20.7) in the pedicle screw group (p= 0.35). There were 15 boys and 18 girls in both groups.
Mean operative times were 7.45 hours (SD ± 2.18; range 3.84-12.5) in the hybrid group and 6.04 hours (SD ± 1.71; range 2.90-10.5) in the pedicle screw group (p= 0.0012) and mean intra operative blood loss 3760 mL (SD ± 2.79; range 350-12000) and 1785 mL (SD ± 1.11; range 230-4400) (p=0.0015). In blood volumes the blood losses averaged 1.7 (SD ±1.3) in the hybrid and 0.82 (SD ±0.49) in the pedicle screw group, respectively (p=0.0070). In patients undergoing anteroposterior surgery, the operative time for the posterior part of the surgery was also significantly shorter for the pedicle screw group as compared with the hybrid (p=0.011), and also intraoperative blood loss was significantly less during the posterior surgery (p=0.0061).

Iliac fixation was carried out more often in the pedicle screw group (p=0.007). There were no differences in the amounts of fused vertebral segments. All ambulatory patients maintained their walking ability. SRS-24 total scores were 97 in the hybrid group and 95 in the pedicle screw group at final follow-up (p=0.41).

Radiographic Outcomes

The baseline patient characteristics of the matched cohorts were similar preoperatively. The mean preoperative Cobb angle of the major curve was 87° (SD ± 29; range 25-141) in the hybrid group and 80° (SD ± 17; range 47-116) in the pedicle screw group (p=0.23). The

preoperative flexibility of the major curves in traction radiographs was similar in the study groups (36% ± 22% in the hybrid vs. 37% ± 14% in the pedicle screw group). The magnitude and correction of major curve was significantly better in the pedicle screw group as compared with the hybrid group at immediate postoperative ($p=0.0028$ and $p<0.001$), six months ($p<0.001$ for both comparisons), and two-year postoperative radiographs ($p=0.0016$ and $p=0.0011$). Average major curve corrections at two years were 59% (range, 37% - 88%) for the hybrid and 75% (range, 43% - 97%) for the pedicle screw group, respectively ($p=0.0011$). (Figure 9).
Eleven patients in both study groups had thoracic hyperkyphosis (>40 degree kyphosis between T5-T12). Preoperatively, thirteen patients in both groups had a positive global sagittal balance (≥20 millimetres) in both groups, and 14 of the hybrid group, and 12 of the pedicle screw group at final follow-up. There were no statistically significant differences of the mean kyphosis and lordosis or sagittal and coronal balances or pelvic obliquity pre- and postoperatively between the study groups (Table II). There was no radiographic evidence of a non-union at follow-up. Proximal junctional kyphosis (>15°) was observed in 13 of the hybrid and in six patients of the pedicle screw group ($p=0.057$). None of our patients needed revision surgery for proximal junctional kyphosis.

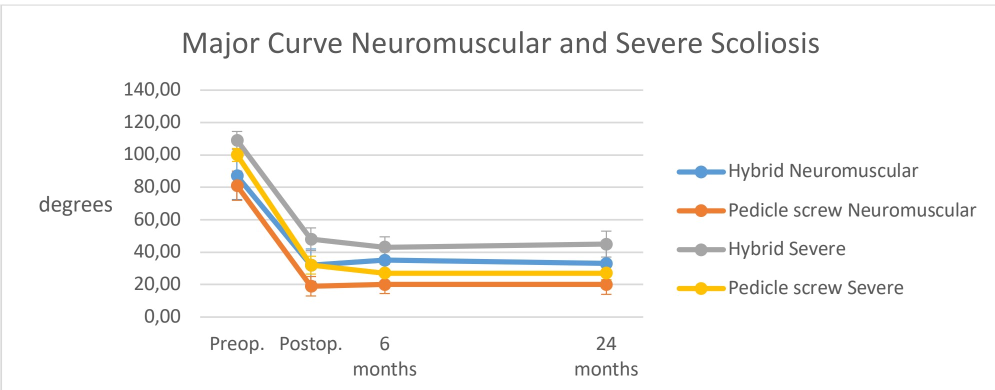

Figure 22. Major Curve in neuromuscular and Severe scoliosis

Health-related quality of life

The SRS-24 total score averaged at two-year follow-up:

- 100.4 (SD ±5.7) points in the N- DVR group
- 99.3 (SD ±9.0) in the DVR group

No significant differences existed in the seven main domains of SRS-24 between the study groups at two-year follow-up.

STUDY III

Clinical findings

The mean age at operation was 15.9 years (range 10.6-20.7) in the Hybrid group and 14.8 years (9.6-19.6) in the Pedicle Screw group (p=0.31) (Table 1). There were 5 boys in the Hybrid and 6 boys in the Pedicle Screw group. Mean operative times were 8 hours 3 minutes (3 hours 48 minutes -12 hours 30 minutes) in the Hybrid group and 6 hours 24 minutes (4 hours 30 minutes – 8 hours 15 minutes) in the Pedicle Screw group (p= 0.015) and mean intra operative blood loss 4300 ml (range 350-12000 ml) and 2700 ml (500-8000 ml) (p=0.14) (Table 13).

The mean implant density per fused vertebral bodies was significantly higher in the Pedicle Screw than in the Hybrid group (2.0 vs. 1.52; p<0.001) (Table 3). Iliac fixation was carried out more often in the pedicle screw group (p=0.014). There tended to be more fused segments in the Pedicle Screw (15.0) as compared with the Hybrid group (14.3) (p=0.074). All ambulatory patients maintained their walking ability

Radiographic Outcomes

The mean preoperative Cobb angle of the major curve was 109° (range, 90°-127°) in the Hybrid group and 100° (90-116°) in the Pedicle Screw group (p=0.015) (Table 12). The preoperative flexibility of the major curves in traction radiographs was similar in the study groups (29% ± 12% in the Hybrid vs. 33% ± 14% in the Pedicle Screw group). The magnitude and correction of major curve was significantly better in the Pedicle Screw group as compared with the Hybrid group at immediate postoperative (p=0.0010 and p=0.0044), six months (p<0.001 and p=0.0017), and two-year postoperative radiographs (p<0.001 and p=0.0023) (Table 12). Average major curve corrections at two years were 59% (range, 37% - 81%) for the Hybrid and 73% (range, 60% - 81%) for the Pedicle Screw group, respectively (p=0.0023) (Fig. 22).

Two patients in the Hybrid and three in the Pedicle Screw had preoperatively thoracic hyperkyphosis (>40 degree kyphosis between T5-T12) (Table 12). Mean thoracic kyphosis was significantly higher in the Hybrid than in the Pedicle Screw group at 2-year follow-up (p=0.034) and lumbar lordosis significantly less in the Hybrid than in the Pedicle Screw group at immediate postoperative radiographs (p=0.013). There were no statistically significant differences of coronal balance or pelvic obliquity pre- and postoperatively between the study groups (Table 12). There was no radiographic evidence of a non-union at follow-up.

Measures	Hybrid (n = 15)	Pedicle screw (n = 17)	Significance (P-value)
Major curve (degrees and percentages, SD)			
Preoperative (, SD)	109 ± 11	100 ± 8	0.015
Major curve on traction film (º)	76 ± 15	67 ± 15	0.13
Correction on traction (%)	29 ± 12	33 ± 14	0.43
Immediate postoperative (º)	48 ± 14	32 ± 11	0.0010
Correction (%)	56 ± 12	68 ± 10	0.0044
Postoperative 6 months (º)	43 ± 13	27 ± 11	<0.001
Correction (%)	61 ± 11	73 ± 9	0.0017
Postoperative 2 years (º)	45 ± 16	27 ± 8	<0.001
Correction (%)	59 ± 14	73 ± 7	0.0023
T5–T12 kyphosis			
Preoperative (º)	46 ± 16	39 ± 33	0.60
Immediate postoperative (º)	29 ± 15	29 ± 9.4	0.90
Postoperative 2 years (º)	33 ± 12	23 ± 9.6	0.034
T12–S1 lordosis			
Preoperative (º)	63 ± 17	57 ± 15	0.54
Immediate postoperative (º)	46 ± 12	59 ± 9	0.013
Postoperative 2 years (º)	49 ± 14	56 ± 9	0.19
Coronal balance (mm)			
Preoperative	44 ± 43	57 ± 26	0.41
Postoperative 2 years (º)	23 ± 19	23 ± 21	0.46
Pelvic obliquity (º)			
Preoperative	22 ± 16	23 ± 12	0.95
Postoperative 2 years	7 ± 6	6 ± 7	0.70

Table 12. Radiographic outcomes, Study III

Complications (studies I-III)

	Study I		Study II		Study III	
Patient/**P**opulation	Thoracis idiop. scoliosis		Neuromuscular scoliosis		Severe scoliosis	
Intervention/**C**omparator	*En bloc*-DVR (n = 48)	Non-DVR (n = 24)	Hybrid	Total pedicle screw	Hybrid	Total pedicle screw
Blood loss (ml)	920 ml (300–2000)	1010 ml (350–2250)	3760 ml (SD ± 2.79; range 350-12000)	1785 ml (SD ± 1.11; range 230-4400)	4300 ml (range 350-12000)	2700 ml (500-8000 ml)
Complications (total)	**4**		**24**	**10**	**7**	**5**
chylothorax					1	
deep wound infection	1		3	1		
dura lesion	1		2	2		1
implant failure			3	2	1	1
loss of MEPs during scoliosis surgery						1
Major gastrointestinal disorders lasting over 10 days			7	1		
nerve deficit	1					
pleural effusion						1
pleural lesion			3			
pneumonia			1	1	1	
pneumothorax	1				1	
pos. sag. balance due to lumbos. junct. kyphosis						1
pos. sag. balance sacral junct. kyphosis				1		
Revision surgery			4	1		
spinal cord deficit					1	
superior gluteal arterial lesion				1		
superior mesenterial artery syndrome					1	
syndr. of inappropriate ADH secretion			1			
urinary retention and urosepsis					1	

Table 13. Complications and blood loss

The implant failures included

- three rod breakages just above iliac connector
- one iliac connector breakage
- one hook claw cutting through the laminas
- Only one of these patients (hybrid group) has required revision surgery at the lumbosacral junction.

Subgroup analysis

In a subgroup analysis, patients with non-neuromuscular scoliosis were excluded. Correction of the major curve was significantly better at six months (mean 60% vs. 73%, p=0.0020) and at two-year follow-up in the Pedicle Screw as compared with the Hybrid group (mean 58% vs. 72%, p=0.0059). Operative time tended to be less in the Pedicle Screw than in the Hybrid group (mean 7 hours 40 minutes vs. 6 hours 22 minutes, p=0.074).

STUDY IV

Clinical findings

Eight children with upper cervical instability due to skeletal dysplasia underwent cervical spine stabilization with or without decompression in Helsinki ja Turku University Hospitals. Various surgical methods were practiced.

- Brooks-Jenkins wiring
- C1/C2 transarticular screws
- C0-C3 spondylodesis with metal wiring
- Occipitocervical fusion with Axon, USS, Vertex Max and Legacy instrumentations
- C4 corpectomy
- C1 lateral mass and c2 pedicle screw technique (Harms technique)

Clinical and radiological Outcomes

Patients 1 and 2. C1/C2 fusions were performed for two girls with Spondyloepiphyseal dysplasia (SED) aged 4 and 7 years, respectively. C1/C2 transarticular screw fixation was preferred preoperatively for both. The first patient had atlantoaxial instability (8 mm) and a hypoplastic dens on flexion–extension magnetic resonance (MR) images. During the operation patient nro 1 encountered left-sided vertebral artery tapping and thus the method was changed sublaminar wire fixation according to Brooks and Jenkins.

Patient 2 at the age of 3 years presented with a hypoplastic C2 vertebra and a 5-mm instability during flexion–extension radiographs. At follow ups the instability increased, and one-sided C1/C2 transarticular fixation was operated. The other side was left intact because of a high-riding vertebral artery. Fixation was strengthened using Brooks–Jenkins type sublaminar wires and autologous iliac bone graft. Both patients were immobilized using halo body jacket for 4 months, and solid spinal fusion could be verified radiologically during follow-up.

Patient 3 was also diagnosed Spondyloepiphyseal dysplasia. For C1/C2 instability, he underwent a C1 laminectomy and a C0–C2 spondylodesis using metal wires at the age of 5 years. At the age of 15 years, he presented with fatigue in the lower extremities and left upper arm. Radiographs showed implant failure with upper cervical instability. He underwent C0–C2 re-decompression and instrumented occipitocervical fixation. A single structural rib autograft was used with recombinant human BMP-2 (rhBMP-2) (InductOs; Pfizer Inc, New York, NY, USA (off-label use)). Postoperatively, he wore a halo body jacket for 3 months followed by a cervical brace for 1 year. On follow-ups, he has remained symptom-free regarding his cervical spine.

Patient 4 has chondrodysplasia punctata with mild tetraparesis since birth. MR images showed mid- cervical instability with significant high-intensity medullar lesions on T2-weighted images. At the age of 5 years, C4 corpectomy for anterior spinal cord decompression was performed, and spinal fusion was attempted using autologous structural iliac graft with anterior biodegradable plate fixation for reconstruction at another hospital. Immediately postoperatively, the fixation failed and he became tetraplegic. He was transferred to our unit, where, on the first postoperative day, he underwent posterior decompression C2/3–C6/7 with occipito-cervico-thoracic fusion (C0–Th5) using CerviFix with Universal Spine System (USS) pediatric (Synthes GmbH, Zuchwil, Switzerland) and posterolateral autologous bone grafting. This patient did not have a Halo-Jacket support due to severe respiratory distress. He was mobilized supporting the cervical spine with using a custom-made hard collar. His postoperative rehabilitation was uneventful, and his locomotive skills improved accordingly. At 12 months postoperatively, he was able to walk assisted and lift his arms head-height. At 22 months postoperatively, however, the instrumentation had failed at the cervicothoracic region leading to cervical flexion. Second reoperation was performed where the occipitocervical spine was fused using a single autologous rib graft and rhBMP-2. In the operation re-cervicotomy with anterior decompression C3–C6 with reconstruction with autologous bone graft (iliac crest) was performed. Postoperatively, he wore a halo body jacket for 3 months, followed by a cervical brace. On follow-ups, he is walking assisted, performs fine motor skills manually, and solid spinal fusion has been verified using radiographs.

Patient 5 was diagnosed with OI type III. Basilar invagination associated with foramen magnum stenosis, Chiari-I malformation, and mild hydrocephalus was detected at the age of 7 years. He did not present any symptoms, neurological exams were normal, and SSEP was normal. However, he felt that his exertional levels were declining. Surgery was elected, and he had a halo traction for 5 days preoperatively. C1 laminectomy was performed, with decompression of the foramen magnum with occipito-cervico-thoracic instrumentation from C0 to Th5 using occiput plates, cervical hooks, lateral mass screws, and thoracic pedicle screws (Axon; Synthes) with slight lifting of occiput from cervical spine. A posterolateral spondylodesis with allogenic bone grafting was performed. Postoperatively, he wore a halo vest for 3 months, followed by a cervical brace. He fell from his wheelchair 2 days after halo body jacket removal, and one of the stabilizing cervical rods broke. During follow-up, he developed a 50° thoracolumbar kyphoscoliosis needing posterior instrumented total pedicle screw fixation from upper thoracic spine (continuing previous instrumentation with dominos) to L5 (CD Legacy 5.5; Medtronic, Memphis, TN, USA). Two and half years postoperatively, the other cervical rod failed and basilar invagination presented. Halo traction was immediately instituted. A posterior revision using instrumentation from occiput to upper thoracic spine taking advantage of previous fixation points was performed using a single rib strut autograft between occiput and upper cervical spine; rhBMP-2 (InductOs) was applied. Postoperatively, he was immobilized using halo body jacket and with a custom-made collar thereafter. Solid fusion was verified radiologically during follow-up.

Patient 6 is a 16-year-old girl with metatropic dysplasia who had C0/C2 marked instability (C1 assimilation to C0) and cervical spinal cord compression on MRI. The medulla was compressed without signal changes on T2 images. Besides neck pain, she was asymptomatic. Posterior decompression with C1 laminectomy and partial C2 undercutting decompression were performed with C0–C4 instrumented fusion (Vertex Max; Medtronic) using occiput plates and cervical laminar hooks. Autogenous bone grafting from posterior iliac wings and a single dose of rhBMP-2 (InductOs) for spinal fusion were applied. Postoperatively, she used a halo body jacket for 4 months followed by a custom made hard collar.

Patient 7 had diastrophic dysplasia and tetraparesis including respiratory problems since birth. She had a 76° cervical kyphosis on MR images with severe cord compression at C3 level at the age of 3 months. Circumferential cord decompression with anteroposterior cervical spine fusion from occiput to lower cervical spine was attempted at the age 12 months. Autologous fibular strut graft was used anteriorly and allogenic bone graft posterolaterally. Her symptoms did not improve, and she died soon after surgery due to respiratory complications.

Patient 8 presented with C1/C2 instability due to metaepiphyseal chondrodysplasia. Stabilization was performed with C1 lateral mass screws and C2 pedicle screws, augmented with autologous iliac crest bone grafts at the age of 6.5 years without peri- or postoperative complications. Postoperative immobilization was with a halo body jacket, followed by a custom-made collar.

Complications

Six out of seven patients survived through the immediate post-operative period. One patient out of eight died soon after attempted cervical cord decompression and fusion at an early age. One patient (#4) developed significant neurologic deterioration after anterior medullar decompression (C4 corpectomy) and biodegradable plate fixation. Three of four occipitocervical fusion, all without strut autografts or rhBMP-2 resulted in non-union and required revision surgery, one of them two and half years postoperatively.

Discussion

Pediatric spine deformities may be life threatening if untreated (Pehrsson et al. 1992) or result into cardiopulmonary compromise, restrictive lung disease or severe deformity (Sucato et al. 2012). Different treatments for scoliosis have been offered for centuries. The incomplete knowledge of the disease has resulted in continuous "try and see" strategy all around the world. Scoliosis as a very visible defect has attracted the interest of doctors for centuries, while more subtle deformities e.g. cervical instability have a shorter history in medical research. Pedicle screw construct is dominating the pediatric spine surgery. Because of its rigid nature, it differs from previous techniques. Research to evaluate this triumph is essential.

Statement of Principal Findings

Rotational component can be corrected efficiently when judging the rotation from radiographs, but no significant difference remained between the two groups in the rib hump when measured manually in the follow-up. Conventional wisdom dictates that scoliosis should be corrected when conservative treatment is not giving reasonable outcome before the deformity exceeds 50^0. Pedicle screw technique seems to be superior in most deformity cases. Also in severe neuromuscular scoliosis patients benefit from total pedicle screw constructs. Although pedicle screw construct is expensive compared to hybrid technique, shorter operative time, somewhat less blood loss, better major curve correction with less need for anteroposterior surgery makes it significantly better option in most deformity cases. Instabilities of the cervical spine may end up in cervical myelopathy or even death. Severe instabilities must be treated individually. Baseline examinations and regular follow-ups are highly recommended in the rare disease bone dysplasia group.

Limitations of the study I

In the consecutive patient comparison, DVR patients were older and there were more males. It is possible that older age and the tendency to more rigid male curves make spinal deformity correction more difficult (Smorgick Y et al. 2019, Helenius I et al. 2005). To overcome this bias in the prospective consecutive follow-up study, an additional matched cohort comparison was performed.

There is probably a learning curve effect in this series, and although the surgical times were the same in the 2 groups, more Ponte osteotomies were performed in the DVR group.

Limitations of the study II

The data presented at study II has been collected via prospective systematic data collection system, although the study design was a retrospective in nature. Selection between hybrid and total pedicle screw instrumentation as well as between anteroposterior vs. posterior only surgery represents more development in the current surgical techniques with a tendency to perform as much surgery via posterior only approach due to the pulmonary complications. This may have influenced also for better correction, less operative time, and less blood loss in the pedicle screw fixation group. Position of the pedicle screws was not routineously checked with CT scans. Thus, only complications caused by malposition of pedicle screws can be reported in the present study. The question when to include pelvic fixation in the correction of neuromuscular scoliosis remains somewhat controversial. More patients received pelvic fixation in the pedicle screw group as compared with the hybrid group. None of the patients in the hybrid group underwent re-operation and pelvic fixation during the 2 years follow-up for adding on.

Despite complete radiographic follow-up rate, unfortunately, SRS-24 questionnaires were missing in 45% patients of the hybrid and 30% of the pedicle screw groups, respectively. Scoliosis Research Society 24 outcome questionnaire is not specifically designed for patients with neuromuscular scoliosis. However, it contains useful patient satisfaction questions, which may help in evaluating subjective patient outcomes. Unfortunately, only 55% and 70% of the hybrid and pedicle screw patients answered the questionnaire. It is possible, although unlikely, that patients who were more satisfied with the results of surgery also filled out more SRS-24 questionnaire than those less satisfied. No patient was lost during the minimum two-year follow-up. The evaluation of the outcome of surgical procedures are still developing in this challenging group. Only radiographic outcomes and an ambiguous posture analyse without clinical outcome measures are not satisfying anymore.

Limitations of the study III

The current study represents a comparative clinical based follow-up study in a consecutive series of patient groups undergoing surgery for severe scoliosis with either hybrid or total pedicle screw instrumentation. The data presented was collected via prospective systematic data collection system, although the study design was a retrospective in nature. Selection between hybrid and total pedicle screw instrumentation as well as between anteroposterior vs. posterior only surgery represents more development in the current surgical techniques with a tendency to perform as much surgery via posterior only approach due to the pulmonary complications. Since the findings of this study represent a single surgeon series, it is possible that the results somewhat reflect the learning curve of the senior surgeon during the study period. The aetiology of scoliosis was mixed in this population. The higher implant density may be one of the explaining factors for enhanced deformity correction in the pedicle screw group as compared with the Hybrid group. Pedicle screw patients had bilateral segmental fixation and also more Ponte osteotomies and pelvic fixations than the Hybrid group. On the other hand, significantly more anterior discectomies were performed in the hybrid group to facilitate spinal deformity correction. These factors may have influenced also for the better correction, less operative time, less blood loss, and more posterior surgery in the pedicle screw as compared with the Hybrid group.

The question when to include pelvic fixation in the correction of neuromuscular scoliosis remains somewhat controversial. More patients received pelvic fixation in the pedicle screw group as compared with the hybrid group. Despite complete radiographic follow-up rate, unfortunately, SRS-24 questionnaires were missing in 40% patients of the hybrid and 30% of the pedicle screw groups, respectively. Scoliosis Research Society 24 outcome questionnaire is specifically designed for patients with adolescent idiopathic scoliosis, and most of these patients had a neuromuscular scoliosis. However, it contains useful patient satisfaction questions, which may help in evaluating subjective patient outcomes. It is possible, although unlikely, that patients who were more satisfied with the results of surgery also filled out more SRS-24 questionnaire than those less satisfied. Since the majority of the patients had a neurologic basic disease with less cognitive ability, the results of the SRS-24 questionnaire need to be considered with caution. No patient was lost during the minimum two-year follow-up.

Limitations of the study IV

The nature of rare skeletal dysplasias defines the study to a case based evaluation. The limited number of cases weakens the statistical evaluation. This retrospective study consisted of eight children with five different rare skeletal dysplasias needing upper cervical instrumented stabilization. Rare skeletal dysplasias may also present the disease in various matters, thus the need for care varies (Jalanko T et.al. 2009).

Comparison with previous findings

Study I

Hwang (Hwang et al. 2012) evaluated effectiveness of DVR on thoracolumbar (Lenke 5C) curves in 34 patients. In agreement with the findings of our study, they were not able to demonstrate any significant differences in the thoracolumbar rib hump or radiographical parameters between the 19 patients operated with DVR and the 15 patients operated without it. The limitations of the study include various DVR techniques (segmental or en bloc or both), multisurgeon design (the details of surgical correction may vary) and the retrospective nature of the study.

Additionally, thoracolumbar rib hump is probably much more flexible and easier to correct than main thoracic rib hump as it locates in the more mobile segment of spine.

It should be noted that also the N-DVR group underwent correction of the spinal deformity using monosegmental thoracic pedicle screws apically, which have been shown to be significantly more effective than multi-axial pedicle screws for rotational correction of AIS (Kuklo TR et al. 2005). This may further decrease the difference between the N-DVR and

DVR groups. Use of transverse connectors has been shown to increase rotational stability of the segmental pedicle screw instrumentation (Kuklo TR et al. 2008). The absence of transverse connectors may have affected the rotational stability of our constructs and thus resulted in partial loss of spinal rotational correction. However, no loss of spinal rotation correction was observed in the DVR group during follow-up.

In contrast with the findings by Hwang (Hwang et al. 2012), flattening of thoracic hypokyphosis did not occur in the DVR group. This flattening tendency was observed only in the N-DVR group. One explanation could be the ability to lift up the low lying main thoracic apical area with the derotation device used in the current study. DVR instruments, which allow not only compression but also lifting up the concave side, may thus increase the possibility to maintain thoracic kyphosis.

Although direct vertebral column en bloc derotation produces immediate rib hump correction at the time of surgery, it seems that some of this correction will be lost during two-year follow-up. Spinal instrumentation is rigid and no loss of correction occurred in the coronal plane. Correction of spinal rotation was significantly better in the DVR as compared with N-DVR group at 2-year follow-up. It is possible that the uninstrumented rib deformity recurs like a spring. Another possible explanation for rib prominence recurrence could be continued thoracic cage growth, which we call as "rib crankshaft". Thoracic cage reaches its final volume of by the age of 15 (Kim YJ, 2004) and over half of our patients were below this age at the time of surgery.

Study II

Arun et al. reported the results of different instrumentation techniques (sublaminar instrumentation vs. hybrid vs. TPS) in 43 patients with Duchenne's dystrophy (Arun R, 2010). Small number of incident cases in the pedicle screw group (11) and hybrid group (13) were a limitation of that study. There was less blood loss and shorter operation time in total pedicle screw instrumentation compared to hybrid constructs, which is in line with our results. Furthermore, our study demonstrated better curve correction in TPS group which was also observed after immediate post-operative correction was subtracted with flexibility index in the study of Arun. Difference in maintaining the achieved curve correction was not observed in our study, where as the achieved curve correction maintained better with pedicle screw group in the study of Arun. Modi et al. reported satisfactory correction of neuropathic scoliosis with total pedicle screw construct in 52 patients with cerebral palsy (Modi 2009). The lack of control group was a limitation in that study. The magnitude of major curve correction from 76.8 to 30.1 was less than in our study with no loss of correction. Tsirikos and Mains (Tsirikos A, Mains E. , 2011) reported scoliosis correction from 83 degrees to 21 degrees and pelvic obliquity from 24 to 4 degrees using all pedicle screws in patients with quadriplegic CP. These figures are clearly higher than those obtained using the third generation CD instrumentation in the same patient group (Teli MG et.al., 2006). In patients with neuromuscular scoliosis, correction of the spinal deformity is less important than for patients with adolescent idiopathic scoliosis and thus the higher radiographic correction of the deformity when using pedicle screws is a positive, but may not be the most clinically relevant finding.

Use of all pedicle screw instrumentation may also reduce the need for anterior surgery by providing better spinal deformity correction due to better biomechanical spinal instrumentation (Ledonio C, 2011) and better control of crankshaft phenomen in patients with open triradiate cartilage (Sponseller P , 2010). It was the authors' standard practice to use pedicle screws bilaterally at every level. Bilateral segmental pedicle screw instrumentation was used to reduce risk of implant pull-out in these patients known to have a poor bone quality. Scoliosis Research Society outcome questionnaire 24 were somewhat better for the hybrid group, although this was far from statistical significance.

Major blood loss and associated coagulopathy are one of the major risk factors for severe complications and deaths in patients undergoing surgery for neuromuscular scoliosis. Therefore, one of the major clinical advantages of pedicle screw constructs over hybrid or Luque-Galvestone instrumentation is limited blood loss. Passing a sublaminar wire or hook into the epidural space may start epidural venous bleeding, which can be difficult to stop and can re-start at every level of instrumentation. In contrast, pedicle screw is an implant, which when optimally placed, does not violate spinal canal. If bleeding starts from the cancellous bone of the vertebral body, it usually stops after screw insertion. Additionally, while pedicle screws may sometimes take longer time to insert than hybrid anchors, many anterior approaches were also avoided. When only posterior approaches were compared, intra operative blood loss was more limited in the pedicle screw than in the hybrid group. In the current series, average blood loss of 1785 ml in the pedicle screw group and 3760 ml in the hybrid group are within the previously reported blood loss ranges (Haher T et.al., 1999; Piazzolla A et.al., 2011).

Master et al. identified nonambulatory status and a preoperative major curve of 60 degrees or more as the significant risk factors for major complications and increased length of hospital stay (Master D et.al., 2011). In his series, 28% of the patients undergoing surgery had major complication, including two deaths. In the series of Modi et al. complication rates (32%) were in the same magnitude than in our study (Modi H et.al., 2011).

Study III

Better radiographic outcomes using Pedicle Screw instrumentation for adolescent idiopathic scoliosis as compared to Hybrid constructs have been published (Watanabe K et al., 2008; Dobbs M et.al., 2006; Kuklo T et.al., 2005; Ledonio C et.al., 2011). Similar comparative studies in patients with severe scoliosis are few. Watanabe et al. (2008) observed better correction of spinal deformities of 100 degrees or more using pedicle screw than hybrid constructs. However, in their series one third of patients operated using pedicle screws had a VCR procedure, which obviously makes comparison less reliable. In the present study, similar number of patients in both groups underwent VCR, but still the correction of the deformities was better using pedicle screw instrumentation. Most of our patients had a neuromuscular scoliosis. In these patients, correction of the spinal deformity is less important than for patients with adolescent idiopathic scoliosis and thus the higher radiographic correction of the deformity when using pedicle screws is a positive finding, but may not be the most clinically relevant finding. On the other hand, correction of the severe neuromuscular scoliosis to allow for better seating, feeding, etc. is as important as the esthetics as the idiopathic curvature of less magnitude.

Kuklo et al (2005) followed twenty patients with idiopathic scoliosis of 90 degrees or more operated using pedicle screw instrumentation. Three patients had an anteroposterior approach. Spinal deformity correction was slightly less in their series (67%) as compared with the current series (73%). Hamzaoglu et al. (2008) reported a mean 51% correction of severe idiopathic scoliosis in 15 consecutive patients who underwent wide posterior facet joint resections and pedicle screw instrumentation combined with intraoperative halo-femoral traction up 50% of body weight.

Koller et al. (2012) reported treatment of severe scoliosis (mean 106°) with preoperative halogravity traction. One-third of their 45 patients underwent open anterior release, but none had VCR. Radiographic correction rate of 33% was much lower than in the current series, but also the mean age of their patients was much higher (24 years vs. 15 years in the current series).

Use of all pedicle screw instrumentation may also reduce the need for anterior surgery by providing better spinal deformity correction due to better biomechanical spinal instrumentation (Ledonio C et.al., 2011) and better control of crankshaft phenomen in patients with open triradiate cartilage (Sponseller P et.al., 2010). Additionally, while pedicle screws may sometimes take longer time to insert than hybrid anchors, many anterior approaches were avoided.

Studies have evaluated mortality in patients with severe scoliosis. Pehrsson et al. (1992) observed increased mortality in untreated patients with scoliosis of 70 degrees or more. Phillips et al. (2013) reported a mortality rate of 18% in patients with syndromic early-onset scoliosis. In the present study, patients with severe scoliosis of 90 degrees or more were followed up to a mean of 5.5 years postoperatively to evaluate the mortality, which was only 3%. All patients with severe scoliosis have a restrictive lung disease (Newton et al. 2005), which according to studies in patients with idiopathic scoliosis is only partially reversible even after major spinal deformity correction (Kim YJ et.al., 2005). Additionally, most of our patients had an underlying neurological disorder. Thus, the low mortality rate suggests relatively well-balanced surgical indications, peri- and postoperative care as well as a well-treated general health in these patients.

Study IV

Ain et al (vuosi) reported outcomes of 25 patients (aged 1.75 to 46.9 years) with skeletal dysplasias undergoing cervical spine fusion. Solid bony union was detected in 21 patient out of 25. This is strikingly different from our series, with only three patients out of seven developing solid bony union. Our patient population included rare skeletal dysplasias with one previous case report available for cervical spine fusion on a patient with chondrodysplasia punctata and one report with 6 cases (3 SED, 1 Morquio's syndrome, 1 pseudoachondroplasia and 1 chondrodystrophia calcificans congenita) and no previous reports for cervical spine fusion in patients with diastrophic dysplasia.

Atlantoaxial instability is known to associate with spondyloepiphyseal dysplasia (SED). Nakamura (Nakamura et al. 1998) evaluated sixteen SED patients (aged from 3 to 37 years). Six (38%) of them showed atlantoaxial instability and five of them changes suggesting myelopathy. Risk factors for cord compression included short stature (-7 SD) and severe coxa vara. Ain (Ain et al 2006) reported seven SED patients with upper cervical spine fusion. Spinal fusion occurred in five patients during follow-up, one patient required revision surgery due to nonunion and one patient presented implant loosening. Three had C1/C2 fusion with two undergoing solid spinal fusion. Svensson and Aaro reported solid fusion in three patients with SED during follow-up (3/3patients) (Svensson et al. 1988).

Chondrodysplasia punctata has been associated with three types of spinal deformities, of which a C2 dentocentral disruption affects the cervical spine. Spinal instability has been reported and a case report with cervical spine stenosis in chondrodysplasia punctata has been previously reported.

From eight to twenty-five per cent of patients with Osteogenesis Imperfecta (OI) develop basilar impression. Ibrahim and Crockard (Ibrahim et al. 2007) reported long-term outcomes of 20 patients (one 12-yr-old child) treated using ventral decompression and staged occipitocervical instrumented fusion. At the end of follow-up 25% of the patients had recurrence of brainstem symptoms or had died, and 15% showed no neurologic improvement.

Leet (Leet et al. 2006) evaluated cervical spine in 13 patients with metatropic dysplasia. Nine had spinal stenosis (SAC < 11 mm). Two children had myelopathy. Atlantoaxial instability (ADI > 5 mm) was additionally noted in five patients. Nine patients underwent posterior upper cervical fusion and decompression of the spinal cord. Three patients developed non-union and four patients developed other complications. In our patient, atlantoaxial instability resulted into fixed anterior position of C1 on C2 and spinal cord compression without neurological compromise. Instrumented occiput-C2 fixation with wide neural element decompression resulted in bony fusion.

CONCLUSIONS

1. In a prospective two year follow-up study with a 100% follow-up rate, we were not able to demonstrate any significant differences in the thoracic rib hump correction in AIS patients undergoing surgery with total pedicle screw instrumentation using DVR as compared with no DVR. DVR may also provide tools to prevent flattening of thoracic kyphosis with all pedicle screw constructs.

2. Total pedicle screw instrumentation provided significantly shorter operative time (1 hour 40minutes), less blood loss (2000ml), better major curve correction (two year follow-up 75% vs 59%) with less need for anteroposterior surgery as compared with hybrid constructs in patients with neuromuscular scoliosis.

3. Mortality rate was low (one patient) up to a mean of five years follow-up. Pedicle Screw instrumentation provided shorter operative time (1 hour 39minutes), less blood loss (average 1600ml), better major curve correction (two year follow-up 73% vs 59%) with less need for anteroposterior surgery as compared with Hybrid constructs in patients with severe over 90 degrees scoliosis.

4. Surgical fixation in the pediatric cervical spine is hampered by small and fragile posterior structures. Upper cervical instability in a patient with skeletal dysplasia must be evaluated and treated individually.

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