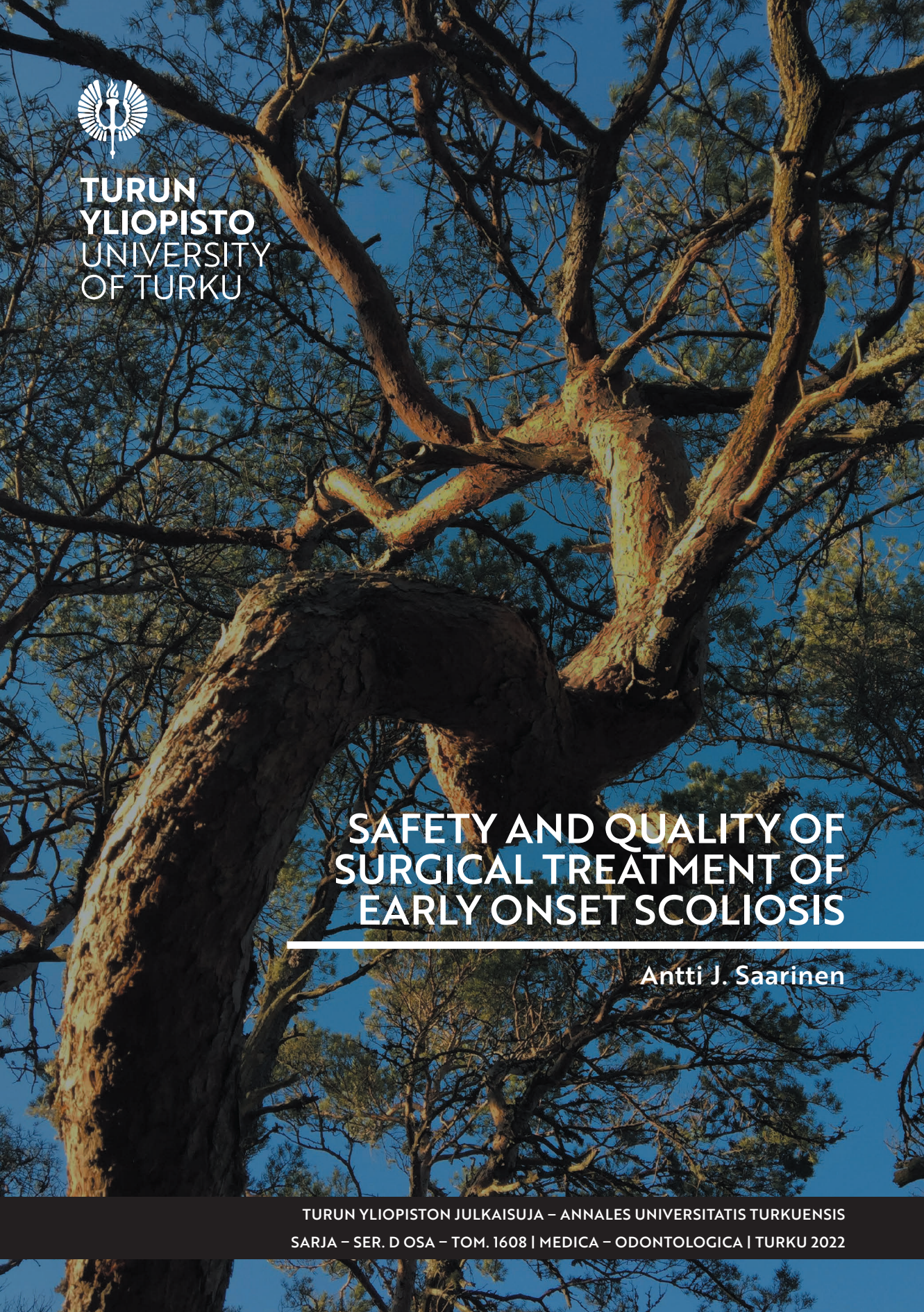

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SAFETY AND QUALITY OF SURGICAL TREATMENT OF EARLY ONSET SCOLIOSIS

Antti J. Saarinen

TURUN YLIOPISTON JULKAISUJA – ANNALES UNIVERSITATIS TURKUENSIS
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Dedicated to all children with scoliosis

UNIVERSITY OF TURKU
Faculty of Medicine
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ANTTI J. SAARINEN: Safety and Quality of Surgical Treatment of Early Onset Scoliosis
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ABSTRACT

Early onset scoliosis (EOS) is defined as abnormal lateral curvature of the spine diagnosed before the age of 10. Untreated EOS is prone to progression and may complicate the normal development of the thoracic cavity and lungs, leading to thoracic insufficiency syndrome. EOS is classified according to the etiology as congenital, neuromuscular, syndromic, or idiopathic early onset scoliosis. Surgical treatment is warranted in severe or progressing EOS. Growth-friendly treatment provides deformity correction while allowing spinal growth.

The aim of this thesis was to study the outcomes of modern surgical treatment of EOS. We compared magnetically controlled growing rods (MCGR) and traditional growing rods (TGR) in severe EOS, compared passive Shilla instrumentation and MCGRs in syndromic and neuromuscular EOS, and studied the effect of growth-friendly surgical treatment in patients with and without growth limiting skeletal dysplasias.

Modern surgical treatment of EOS has improved the outcomes and decreased the incidence of complications. Further research is still needed on the optimal instrumentation selection and planning the treatment especially with children with co-morbidities.

KEYWORDS: early onset scoliosis, congenital scoliosis, neuromuscular scoliosis, syndromic scoliosis, idiopathic scoliosis, growth-friendly treatment

TURUN YLIOPISTO
Lääketieteellinen tiedekunta
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TIIVISTELMÄ

Varhaisiän skolioosi määritellään selkärangan poikkeavana sivuttaissuunnan käyryytenä, joka on todettu ennen kymmentä ikävuotta. Hoitamaton varhaisiän skolioosi on altis etenemään ja voi vaikeuttaa rintaontelon ja keuhkojen normaalia kehitystä johtaen alikehittyneeseen rintaonteloon. Kirurgista hoitoa tarvitaan, kun kyseessä on vaikea käyryys tai etenevä skolioosi. Kasvuystävällinen hoito korjaa selkärangan virheasentoa mahdollistaen samalla selkärangan kasvun.

Vertailimme magneettitankoja ja kirurgisesti pidennettäviä kasvutankoja potilailla, joilla oli vakava varhaisiän skolioosi. Lisäksi vertailimme passiivisen Shilla-instrumentaation ja magneettitankojen tuloksia potilailla, joilla oli syndroomaan liittyvä tai neuromuskulaarinen varhaisiän skolioosi. Tutkimme myös kasvuystävällisen kirurgisen hoidon vaikutusta potilailla, joilla oli kasvua rajoittava luustodysplasia, verrattuna potilaisiin, joilla skolioosiin ei liittynyt dysplasia.

Varhaisiän skolioosin nykyaikainen kirurginen hoito on parantanut hoidon tuloksia ja vähentänyt komplikaatioiden määrää. Jatkotutkimusta tarvitaan yhä parhaan instrumentaation valintaan sekä hoidon suunnitteluun varsinkin niillä potilailla, joilla varhaisiän skolioosiin liittyy muita sairauksia.

AVAINSANAT: varhaisiän skolioosi, synnynnäinen skolioosi, neuromuskulaarinen skolioosi, syndroomaan liittyvä skolioosi, idiopaattinen skolioosi, kasvuystävällinen hoito

Table of Contents

Abbreviations

c-EOS	Classification for Early-onset Scoliosis
EOS	Early onset scoliosis
EOSQ-24	Early onset scoliosis questionnaire 24
HRQoL	Health-related quality of life
MMC	Myelomeningocele
MCGR	Magnetically controlled growing rod
PSSG	Pediatric Spine Study Group
RVAD	Rib-vertebra angle difference
SAQ	Spinal Appearance Questionnaire
SD	Skeletal dysplasia
Shilla	Shilla passive growth guidance instrumentation
SRS-24	The Scoliosis Research Society 24-item questionnaire
TGR	Traditional growing rod
TIS	Thoracic insufficiency syndrome
VACTERL	congenital combination of disorders including vertebral anomalies, anal atresia, congenital heart disease, tracheoesophageal fistula or esophageal atresia, reno-urinary anomalies, and radial limb defect
VEPTR	Vertically extendable prosthetic titanium rib

List of Original Publications

This dissertation is based on the following original publications, which are referred to in the text by their Roman numerals:

I Saarinen A. J., Sponseller P., Andras M., Skaggs D., Emans J., Thompson G., Helenius I., Outcomes of Magnetically Controlled Growing Rods in Severe Early Onset Scoliosis. A Matched Comparison with Traditional Growing Rods. *Journal of Bone and Joint Surgery,* 2021, *Impact Factor: 5.284.*

II Haapala, H., Saarinen, A. J., Salonen, A., & Helenius, I. Shilla Growth Guidance Compared with Magnetically Controlled Growing Rods in the Treatment of Neuromuscular and Syndromic Early-onset Scoliosis. *Spine*, 2020, 45(23), E1604-E1614, *Impact Factor: 3.468.*

III Helenius I., Saarinen A. J., White K. K., McClung A., Yazici M., Garg S., Thompson G. H., Johnston C. E., Pahys J. M., Vitale M. G., Akbarnia B. A., Sponseller P. D. Results of Growth-friendly Management of Early-onset Scoliosis in Children with and without Skeletal Dysplasias: A Matched Comparison. *The Bone & Joint Journal,* 2019, 101(12), 1563-1569, *Impact Factor: 5.082.*

1 Introduction

Scoliosis, derived from a Greek word *skolios* for crookedness, refers to a spinal deformity in which the spine is abnormally curved horizontally. Cobb angle is used to measure the lateral deformity (Cobb 1948). Cobb angle is measured from the superior endplate of the proximal vertebra to the inferior endplate of the distal vertebra of the spinal deformity. Scoliosis is defined as lateral deformity measured with Cobb angle of at least 10 degrees (Cobb 1948). Cobb angle can also be used for measuring kyphosis and lordosis. The modern concept of scoliosis consists of a three-dimensional deformity with possible kyphosis and lordosis as well as associated anomalies, such as fused ribs and spinal rotation (Williams et al. 2014).

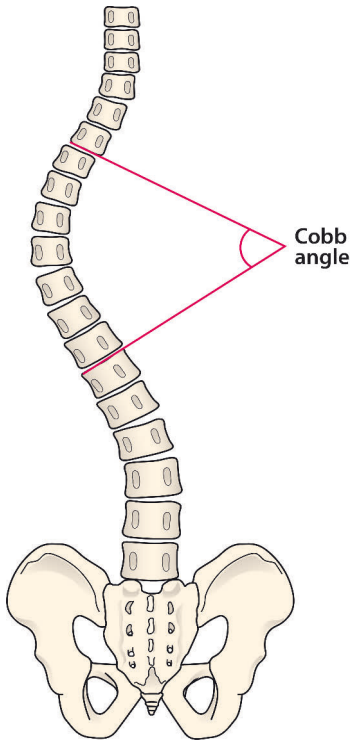

Figure 1. Cobb angle. Based on Cobb, J.R. 1948. Outline for the study of scoliosis. *Instr Course Lect AAOS* 5: p.261–275.

Depending on the age of the patient, scoliosis is classified as early onset scoliosis, adolescent scoliosis, or adult age scoliosis. Early onset scoliosis (EOS) covers a heterogenous group of spinal deformities diagnosed at the age of 10 years or less (Helenius 2018). EOS may appear at birth or develop during growth (Akbarnia et al. 2005). EOS typically progresses during the growth (Akbarnia et al. 2005). Severe spinal deformities at early childhood complicate natural growth and cardiopulmonary development and expose children to further complications, including early death (Pehrsson et al. 1992; Karol et al. 2008). The etiology of EOS is classified as congenital, neuromuscular, syndromic, or idiopathic early onset scoliosis (Williams et al. 2014). EOS is often associated with other developmental comorbidities (Akbarnia 2007).

Conservative treatment of EOS consists of serial casting and bracing, which is used to correct the spinal deformity with natural growth (Mehta 1972; Mehta 2005). Initial surgical treatment of EOS consisted of deformity correction with spinal fusion. However, early fusion prevents growth and limits lung development (Karol et al. 2008). To address this, growth-friendly surgical techniques have been developed (Akbarnia et al. 2005; Cheung et al. 2012; McCarthy et al. 2015).

Surgical treatment with traditional growing rods exposes patients to repetitive surgical procedures and anesthesia, increased risk of wound infections, and reduced quality of life (Bess et al. 2010). More recent treatment methods include magnetically controlled growing rods which allow noninvasive lengthenings and require less operative treatment (Cheung et al. 2012).

This thesis focuses on the surgical treatment of early onset scoliosis. The aims of this thesis are to compare the outcomes of growth-friendly surgical treatment in patients with severe early onset scoliosis, to compare the outcomes of two novel growth-friendly treatment methods, and to study the outcomes of growth-friendly instrumentation on children with skeletal dysplasia.

2 Review of the Literature

2.1 Development of the Spine

2.1.1 Embryological development and fetal period

Spinal formation begins early in the embryonic development, approximately during the third week after the gestation (Kaplan et al. 2005; Akbarnia et al. 2011). Failure in the formation of the early structures complicates the normal development of the spine and may lead to spinal deformities (Kaplan et al. 2005). During the third week, a groove develops in the two-layered cell structure, the bilaminar germ disc, and forms the cranial-caudal axis of the embryo (Akbarnia et al. 2011). Together with other early structures, this groove, also known as the primitive groove, forms the primitive streak along which the remaining axes are formed (Akbarnia et al. 2011). At this point, a three-layered embryo is formed via proliferation and migration of cells (Akbarnia et al. 2011). The layers are called endoderm, mesoderm, and ectoderm (Akbarnia et al. 2011). Notochord is developed from the mesoderm and proceeds to induce the formation of the sclerotomes from the semites (Kaplan et al. 2005). Sclerotomes form the early cartilaginous vertebrae body and arch during the sixth week after the gestation (Kaplan et al. 2005). Two early ossification centers develop in the vertebral body which then fuse in a single one called centrum (Goldstein et al. 2005). Hemivertebrae develops when one of these ossification centers fails to develop, resulting in congenital scoliosis (Goldstein et al. 2005). Vertebral arch is formed from two separate ossification centers (Goldstein et al. 2005). The ossification begins during the eighth week after the gestation and continues through the fetal period (Kaplan et al. 2005).

2.1.2 Development during the early childhood

At birth, vertebrae consist of three ossificated parts joined together with cartilage which allows growth of the spinal canal (Kaplan et al. 2005). The spine grows rapidly during the first five years, approximately two centimeters a year (Dimeglio et al. 2012). Spinal growth then slows down to one centimeter a year until approximately the tenth year (Dimeglio et al. 2012). A second phase of rapid growth

follows during the puberty, during which adolescent scoliosis may develop (Dimeglio et al. 2012). In all, spinal height will double during growth (Dimeglio et al. 2012).

During the fetal period, the embryo has a c-shaped kyphotic curvature (Kaplan et al. 2005). After birth, the kyphosis persists in the thoracic spine, but lumbar lordosis and cervical curvature develop (Kaplan et al. 2005). Lumbar lordosis develops secondarily after the start of supporting the head (Kaplan et al. 2005).

Lungs and alveoli develop rapidly during the early childhood, with most of the alveoli developing during the first two years (Dimeglio et al. 2012). It is hypothesized that restricted thoracic volume could weaken the normal lung development (Campbell Jr et al. 2007).

Normal pulmonary function requires sufficient lung volume and movement of thorax and diaphragm (Redding 2014). Early onset scoliosis may lead to restrictive lung disease by decreased lung volume, increased rigidity of thoracic cavity, and abnormal function of the diaphragm (Redding 2014; Gillingham et al. 2006). Thoracic volume is complicated in EOS by a three-dimensional deformity including scoliosis, kyphosis, and lordosis, and structural anomalies such as spinal rotation, rib hump, and fused ribs (Campbell Jr, Smith, et al. 2003). Reduced thoracic volume deteriorates the vital capacity, the maximum inhale volume (Karol et al. 2008). Rigidity of the thoracic cavity may be increased by stiff thoracic structures and rib anomalies (Campbell Jr, Smith, et al. 2003). Fused or missing ribs may lead to an abnormally stiff thoracic cavity, which complicates the function of respiratory muscles and steers the patient towards breathing with diaphragm development (Campbell Jr, Smith, et al. 2003). Normal diaphragm function may also be further complicated due to the spinal deformity development (Redding 2014). Neuromuscular co-morbidities participate in deteriorated respiratory muscle work (Tzeng et al. 2000).

Thoracic insufficiency syndrome (TIS) is a severe condition in which the reduced thoracic volume is not able to support normal growth and development, and which ultimately leads to a restrictive lung disease (Campbell Jr, Smith, et al. 2003). TIS was first described in patients with congenital scoliosis or fused ribs (Campbell Jr, Smith, et al. 2003). Clinical assessment, native and computer tomography imaging, pulmonary function tests, and laboratory tests are used in diagnosing TIS (Campbell Jr, Smith, et al. 2003). TIS leads to complicated ventilation and poor quality of life (Olson et al. 2015; Vitale et al. 2008). Untreated TIS leads to increased risk for cardiorespiratory failure after the age of 20 years and increases mortality (Pehrsson et al. 1992). Modern growth-friendly treatment of EOS aims at preventing TIS by correcting the deformity while allowing spinal growth (Campbell Jr, Smith, et al. 2003). Thoracic height of 18 cm is thought to lead to 45% of normal lung function which prevents cardiorespiratory failure (Karol et al. 2008; Gillingham et

al. 2006). Thoracic height of 18 cm equates the normal lung volume of a healthy five-year-old child (Karol et al. 2008).

Early onset scoliosis is prone to progress due to rapid growth during the first years of the childhood (Fernandes et al. 2007). For this reason, early identification and treatment is important in these patients. Delaying the initial surgical treatment reduces the risks for complications by potentially shortening the length of the surgical treatment, allowing the child to grow and develop, and reducing the number of procedures (Fletcher et al. 2012; Bess et al. 2010). Complications are frequent during the surgical treatment of EOS (Bess et al. 2010). Complications often include infections and instrumentation failures (Bess et al. 2010). Surgical treatment is indicated when scoliosis progresses over 50°, as these deformities are likely to further progress to severe deformities (Akbarnia et al. 2005).

In a study by Nissinen et al., the prevalence of scoliosis in patients with average age of 10.8 years was 4.1% (Nissinen et al. 1989). Natural history of EOS is not well known, as cases of untreated patients are scarce. Pehrsson et al. reported elevated mortality within patients with untreated EOS when compared to healthy individuals (Pehrsson et al. 1992).

2.2 Etiology, co-morbidities, risk factors

2.2.1 Classification

In 1954, James classified pediatric scoliosis as infantile (ages 0–3), juvenile (ages 3–10), and adolescent (ages 11 to skeletal maturity) scoliosis depending on the age at the diagnosis (James 1954). Better understanding of the spinal growth and the etiologies have led to the modern classification of paediatric scoliosis to early onset and adolescent scoliosis. Early onset scoliosis covers a heterogenous population of children with a wide range of diagnoses and co-morbidities. To guide treatment of patients with different etiologies, a classification has been developed (Williams et al. 2014). The Classification for Early-onset Scoliosis (C-EOS) classification includes age as a continuous variable, three categorical variables (etiology, major curve angle, kyphosis), and an additional annual progression ratio modifier which utilizes two major curve measurements approximately six months apart (Williams et al. 2014; Cyr et al. 2017) (Table 1).

Table 1. Williams's classification of early onset scoliosis.

Age	Etiology	major curve angle	Kyphosis	Annual progression ratio modifier
Continuous Prefix	Congenital	1: <20°	(-): <20°	P^0: <10° /year
	Neuromuscular	2: 20–50°	N: 20–50°	P^1: 10–20° /year
	Syndromic	3: 51–90°	(+): >50°	P^2: >20° /year
	Idiopathic	4: >90°		

2.2.1.1 Congenital early onset scoliosis

Congenital scoliosis is caused by a developmental error during the fetal phase leading to a structural anomaly (Campbell et al. 2003). Congenital scoliosis may be caused by both failure in formation and failure in segmentation during the development of the vertebra (Hedequist et al. 2007). The most common cause of congenital scoliosis is a failure in the formation of the vertebra. This is caused by failure in the formation of early ossification center leading to defective vertebra. Failure in the formation may be incomplete, leading to a so-called wedge vertebra with both pedicles but asymmetrical height of the sides, or complete failure leading to a hemivertebra which lacks the other half of the vertebra (Hedequist et al. 2004). Failure in the segmentation of the vertebrae may lead to a boney bar which prevents the normal growth in the respective side (Hedequist et al. 2007). Depending on the working growth plates, the deformity caused by congenital scoliosis may rapidly progress along with the growth (Hedequist et al. 2004). Congenital scoliosis with associated hemivertebra can be treated with hemivertebrectomy, in which the abnormal vertebra is removed surgically (Oksanen et al. 2021).

Congenital scoliosis may be associated with missing or fused ribs (Hedequist et al. 2004). Langenskiöld and Michelsson reported significant progressive scoliosis in rabbits after unilateral resection of ribs (Langenskiold et al. 1961). Missing ribs complicate breathing and add to thoracic asymmetry. Fused ribs complicate normal growth and may cause scoliosis (Hedequist et al. 2004). Secondary scoliosis after thoracotomy has been reported (Wong-Chung et al. 1992; Korovessis et al. 1993). Congenital and syndromic early onset scoliosis are associated with obstructive lung disease due to airway compression (McPhail et al. 2013). Congenital scoliosis is often associated with other developmental anomalies (Hedequist et al. 2004). VACTERL association is a combination of congenital disorders including vertebral anomalies, anal atresia, congenital heart disease, tracheoesophageal fistula or esophageal atresia, reno-urinary anomalies, and radial limb defect (Rittler et al. 1996). VACTERL is often associated with congenital scoliosis (Hedequist et al. 2004).

2.2.1.2 Neuromuscular early onset scoliosis

In neuromuscular diseases, the muscle tone is abnormally high (hypertonia) or low (hypotonia, paralysis) (McCarthy 1999). Neuromuscular diseases include cerebral palsy, myelomeningocele, spinal muscular atrophy, and Charcot-Marie-Tooth disease (Berven et al. 2002; Gillingham et al. 2006). Depending on the etiology, neuromuscular diseases may be classified as central, peripheral, mixed central and peripheral, motor endplate, or muscular causes. Ambulatory status may vary depending on the neuromuscular disease. Asymmetric muscle tone causes one-sided force to the trunk: compression force on the growth plate decreases and distraction forces increases growth. This asymmetric force across the spinal column may lead to scoliosis which often worsens during growth. A long deformity extending from sacrum to thoracic level is typical for neuromuscular scoliosis. Neuromuscular diseases may also cause abnormal pelvic obliquity which may cause compensational scoliosis (Vialle et al. 2013). Scoliosis is common in neuromuscular diseases (Table 2).

Myelomeningocele (MMC) is a developmental disorder in which both neural elements and elements protrude from an abnormal opening in the vertebra (Shaer et al. 2007). MMC leads to a neurological defect depending on the level of the disorder (Shaer et al. 2007). Patients with MMC often have neuromuscular scoliosis resulting from the congenital paraplegia (Shaer et al. 2007). MMC related scoliosis has both neuromuscular and congenital traits but is classified as neuromuscular scoliosis (Wild et al. 2001).

Severe scoliosis in non-ambulatory patients may expose them to decubitus, disturb the sitting position, and complicate movement with wheelchair (Majd et al. 1997). Pelvic fixation can be used in non-ambulatory and minimally ambulatory patients (Douleh et al. 2021).

Table 2. Typical neuromuscular diseases and the prevalence of scoliosis according to Berven et al. 2002.

Disease	Scoliosis prevalence (%)
Cerebral palsy	25
Myelodysplasia	60
Spinal amyotrophy	67
Friedreich's ataxia	80
Duchenne myopathy	90
Medullary lesion	100

2.2.1.3 Syndromic early onset scoliosis

Several developmental syndromes are associated with early onset scoliosis, such as Marfan syndrome, Down syndrome, Ehlers-Danlos syndrome, and osteogenesis imperfecta (Levy et al. 2015). While these syndromes are relatively rare, the incidence of scoliosis is higher than in the non-syndromic population (Levy et al. 2015). Developmental syndromes often include various co-morbidities, which further complicate the surgical interventions (Levy et al. 2015). Syndromes like Marfan syndrome, Ehlers-Danlos syndrome, and osteogenesis imperfecta affect the development of the connective tissue and often result in loose joints and scoliosis. Skeletal dysplasias are syndromic diseases which lead to shortened height and often include scoliosis (White et al. 2020).

Marfan syndrome is the most common cause of syndromic early onset scoliosis (di Silvestre et al. 2005). Marfan syndrome is caused by a mutation in the fibrillin-1 gene which causes developmental errors in the connective tissues (di Silvestre et al. 2005). Approximately 60% of the patients with Marfan syndrome have scoliosis and 40% have extensive kyphosis (Levy et al. 2015).

Down syndrome is caused by the trisomy of the chromosome 21 with an occurrence of approximately 1 per 800 births (Bull 2020). Down syndrome causes developmental disability, shortened height, and muscular hypotonia (Bull 2020). Scoliosis is reported in between 7% and 50% of the patients with Down syndrome (Merrick et al. 2000; Levy et al. 2015).

Ehlers-Danlos syndrome is caused by an error in the collagen protein causing heterogenous connective tissue disorder (Mao et al. 2001). Ehlers-Danlos syndrome is associated with hyperextensibility of the skin and hypermobility of the joints (Mao et al. 2001). Scoliosis is present in approximately 23–52% of the patients with Ehlers-Danlos syndrome (Stern et al. 2000; Stanitski et al. 2000).

Osteogenesis imperfecta is caused by abnormal function of collagen I (Martin et al. 2007). Osteogenesis imperfecta is associated with decreased bone quality and increased risk for fractures (Martin et al. 2007). Approximately 50% of patients with osteogenesis imperfecta have scoliosis (Anissipour et al. 2014).

2.2.1.4 Idiopathic early onset scoliosis

Idiopathic scoliosis is used to describe a scoliosis deformity without a specific underlying etiology (Gillingham et al. 2006). Idiopathic EOS can be divided into infantile and juvenile idiopathic scoliosis (Dobbs et al. 1999). Infantile scoliosis is defined as scoliosis diagnosed before the age of three (Dobbs et al. 1999). Juvenile scoliosis is used to describe scoliosis diagnosed between ages three and ten (Dobbs et al. 1999). Mild infantile idiopathic scoliosis associated with plagiocephaly may resolve by itself (Fernandes et al. 2007). Infantile idiopathic scoliosis may resolve

with conservative treatment (Mehta 1972). Reduced lung volumes are common in children with idiopathic EOS (McPhail et al. 2015).

2.3 Conservative treatment

Initial treatment with serial casting and bracing is used for correcting minor deformities and delaying the surgical treatment in more severe deformities (Fletcher et al. 2012; Baulesh et al. 2012; Gussous et al. 2015). Operative treatment in patients under the age of four years increases the risk for complications during the growth-friendly treatment (Bess et al. 2010). Delaying the surgical intervention using conservative treatment lowers the incidence of complications while preventing the progression of the deformity (Fletcher et al. 2012). Infantile idiopathic scoliosis has been shown to resolve with conservative treatment (Mehta 2005; Sanders et al. 2009). Sanders et al. reported resolving of infantile idiopathic scoliosis with serial casting in patients with major curves under 60° (Sanders et al. 2009). Mehta reported long-term results of two groups of patients treated with serial casting (Mehta 2005). Patients treated in an early phase with a mean curve of 32° (mean age 1 year 7 months) resolved with conservative treatment and did not require operative treatment during the follow-up. The second group included patients who had larger curves (mean 52°) and were older (mean 2 years 6 months). In the second group, conservative treatment was able to delay the surgical intervention to the mean age of 12 years and three months.

2.4 Surgical treatment with growth-friendly implants

According to the current evidence, surgical treatment is indicated in severe deformities of at least 50° or progressive deformities which do not respond to conservative treatment (Akbarnia et al. 2005; Akbarnia 2007). Rib-vertebra angle difference (RVAD) can be used to define progressive early onset scoliosis (Mehta 1972). RVAD of 20° or more refers to progressive scoliosis, while deformities with RVAD under 20° may resolve with conservative treatment. Spinal fusion prevents additional thoracic growth and may lead to thoracic insufficiency syndrome. To address this, growth-friendly instrumentations have been developed for deformity correction while allowing thoracic growth. Thoracic height of 18 cm measured from T1 vertebra to T12 vertebra is considered as satisfactory, as this provides 45% of the normal lung volume and improves the survival (Karol et al. 2008). In a classification by Skaggs et al., growth-friendly instrumentations are divided in distraction-based, growth-guidance based, and compression-based (Skaggs et al. 2014). Distraction-based instrumentations apply mechanical force on the spinal deformity. Distraction

force stimulates spinal growth (Mehlman et al. 1997). Initial distraction-based instrumentations required repetitive surgical lengthenings. To address this, non-invasively lengthened instrumentations such as magnetically controlled growing rods have been developed (Cheung et al. 2012). Growth-guidance based instrumentation is a passive method without distraction force (McCarthy et al. 2015). Growth-guidance systems require no surgical lengthenings. Compression-based instrumentation can be used to apply compression force on the convex side of the deformity, which corrects the deformity by decreasing the growth (Skaggs et al. 2014).

2.4.1 Traditional growing rods (TGRs)

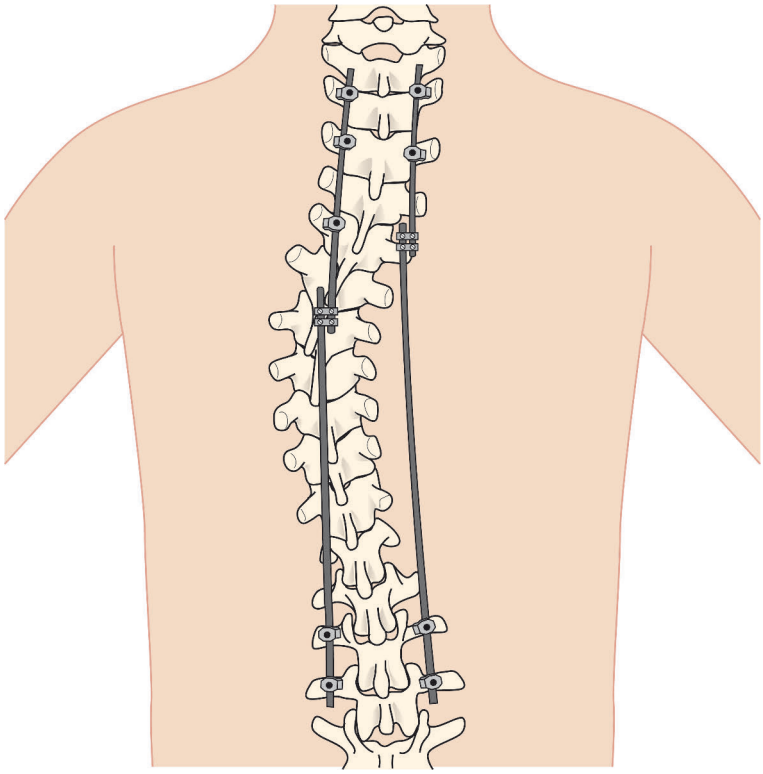

Figure 2. Traditional growing rods. Illustration adapted from Growing Spine Foundation.

Growing rod instrumentation as a treatment for EOS was first described by Harrington in the 1960s (Harrington 1962). Akbarnia et al. described the modern dual rod construct, which is considered as the gold standard (Akbarnia et al. 2005;

Thompson et al. 2005). Single rod constructs are still used in patients with difficult anatomies.

Growing rods are installed using single or dual midline incisions (Akbarnia et al. 2005). Rods are attached to the spine using pedicle screws or hooks. The number of anchors depends on the location and type of the major curve, size and age of the child, and etiology. Pelvic fixation can be used in non-ambulatory patients. Much of the deformity is corrected during the insertion of growing rod instrumentation. TGRs require surgical lengthening usually every six months (Akbarnia et al. 2008). Lengthening is executed through a small incision to expose the lengthening mechanism. Posterior final fusion is often done at the end of the treatment to achieve further deformity correction. Treatment with growing rods is usually finished with posterior spinal fusion, commonly referred to as final fusion (Akbarnia et al. 2005; Poe-Kochert et al. 2016). Complications requiring revision surgery have been reported in 20% of patients after the final fusion (Poe-Kochert et al. 2016).

Repetitive surgical procedures and anesthesia are linked to high complication rates and a high incidence of deep wound infections (Bess et al. 2010; Akbarnia et al. 2005; Farooq et al. 2010). Bess et al. reported at least one complication in 58% of the patients treated with growing rods. The risk of complications increases with every surgical procedure, with one study proposing additional risk of 24% per procedure (Bess et al. 2010). The risk of deep surgical infections is reported to be as high as 50% when patients have reached eight surgical lengthenings (Kabirian et al. 2014). The risk was further increased in non-ambulatory patients, patients with revision surgeries, and patients with stainless steel implants (Kabirian et al. 2014). Delaying the initial procedure decreases the risk for complications (Fletcher et al. 2012; Bess et al. 2010). Bess et al. reported a 13% decrease in complications per delayed year (Bess et al. 2010). Mechanical complications include rod fractures and anchor failures (Yang et al. 2011). Continuous distraction force may lead to autofusion which limits the spinal growth and deformity correction (Cahill et al. 2010; Sankar et al. 2011).

2.4.2 Vertically extendable prosthetic titanium ribs (VEPTR)

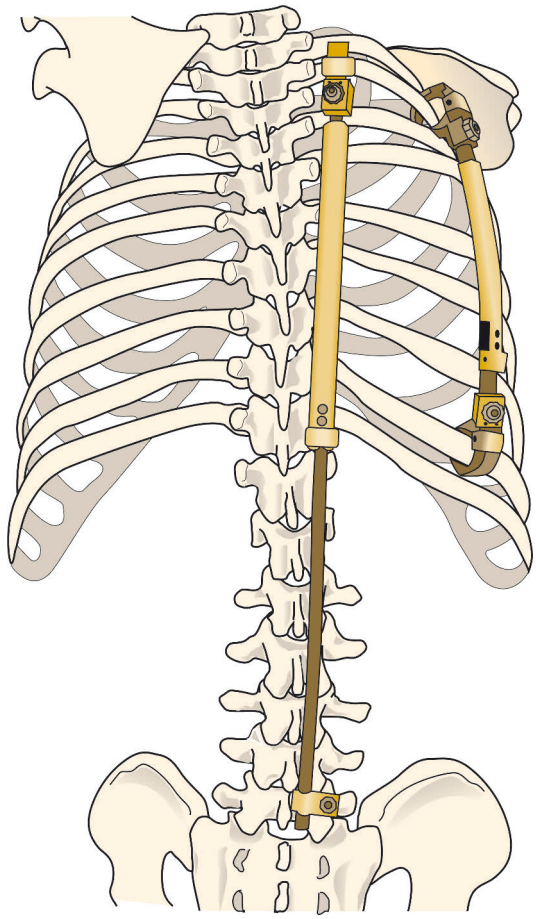

Figure 3. VEPTR instrumentation. Illustration adapted from DePuy Synthes Inc.

Treatment of thoracic insufficiency syndrome (TIS) using expansion thoracoplasty with VEPTR was described by Campbell et al. in 2003 (Campbell Jr & Hell-Vocke 2003). It was first used in congenital scoliosis with associated rib abnormalities. Since then, VEPTR has been proved to successfully treat early onset scoliosis without rib abnormalities (Flynn et al. 2013; El-Hawary et al. 2016; El-Hawary et al. 2020). VEPTR is based on longitudinal distraction of ribs in the concave side of the deformity, which enlarges the thoracic cavity. VEPTR is attached rib-to-rib, rib-to-spine, or rib-to-pelvis. Lengthenings are done surgically.

2.4.3 Magnetically controlled growing rods (MCGRs)

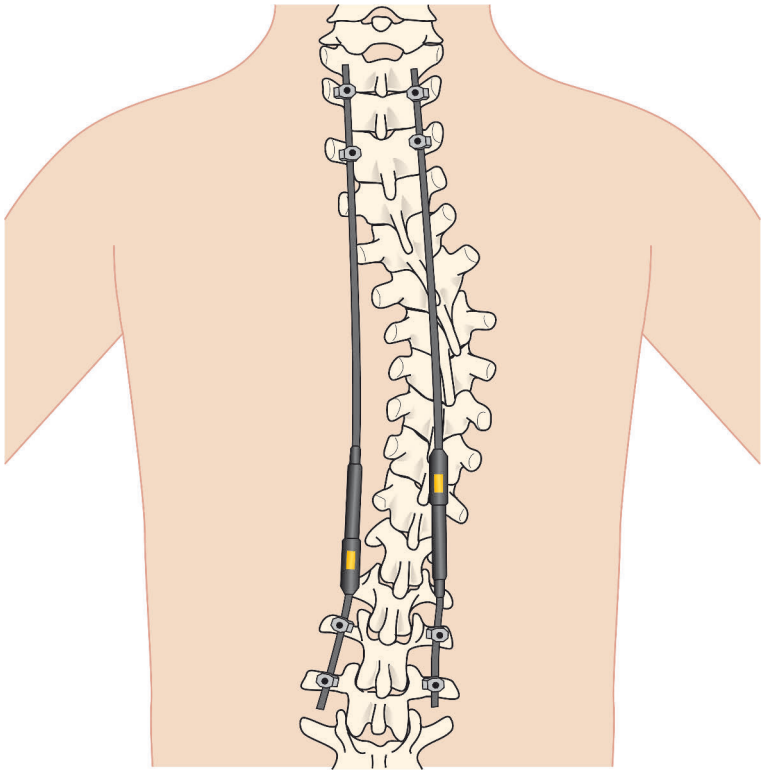

Figure 4. MCGR instrumentation. Illustration adapted from NuVasive Inc.

To address the repetitive surgical procedures of the traditional growing rods, MCGRs were developed (Cheung et al. 2012). MCGRs are installed in a similar way as the TGRs. Both dual and single rod constructs have been used, of which the dual rod construct is considered desirable. Conversion from TGRs to MCGRs leads to similar deformity correction but less spinal growth, possibly due to the law of diminishing returns (Keskinen et al. 2016). Lengthening is done using an external adjustment device usually in a three-month interval. Lengthening requires no anesthesia and is performed in an out-patient clinic setting. Lengthening of the MCGR instrumentation is considered painless (Skov et al. 2020). Frequent lengthenings mimic natural growth better than the six-month cycle used in the TGRs.

First generation MCGRs had mechanical shortcomings, often leading to complications such as loss of distraction (Cheung et al. 2021; Kwan et al. 2017). This was addressed with a revised distraction mechanism (Cheung et al. 2019). Reduced need for surgical procedures decreases deep wound infections (Kar H. Teoh et al. 2016). MCGRs have a large diameter and actuator size, which may prevent

treatment in extraordinarily small or skinny children. MCGRs actuator cannot be contoured, which may prevent implantation in children with very difficult deformities. Metallosis has been found in explanted MCGRs (K. H. Teoh et al. 2016; Zhang et al. 2020). The long-term effect of metallosis is not known.

Previous results of treatment with MCGRs have shown satisfactory deformity correction and thoracic growth (Dannawi et al. 2013; Hickey et al. 2014; Hosseini et al. 2016; Lebon et al. 2017; Lebel et al. 2021). Akbarnia reported similar deformity correction, thoracic growth, and rate of complications in patients treated with MCGRs and matched patients treated with TGRs (Akbarnia et al. 2014). Lebel et al. reported a high rate of unplanned revision surgeries of 45% in their study (Lebel et al. 2021). According to their findings, the need for unplanned revision correlated with thoracic kyphosis over 40 degrees. Fewer surgical procedures result in a lower incidence of deep surgical infections in the MCGRs (Choi et al. 2017). The higher initial cost of the MCGR is compensated during the growth (Rolton et al. 2015; Polly Jr et al. 2016).

The need for significant contouring may complicate the installation of the MCGR instrumentation. This may prevent the treatment in extremely skinny patients or in patients who have difficult deformities. MCGR may not be suitable in patients who require repetitive magnetic resonance imaging or who have pacemakers. In these patients, TGRs are often used (Varley et al. 2021).

2.4.4 Pedicle screw trolley instrumentation (Shilla)

The pedicle screw trolley instrumentation (Shilla) was first described by McCarthy (McCarthy et al. 2010; McCarthy et al. 2014; McCarthy et al. 2015). It presents a passive growth guidance without distraction force by guiding natural growth using sliding screws. Due to the passive guidance, Shilla instrumentation does not require additional surgical procedures after initial implantation and final fusion. Shilla instrumentation has been reported to provide similar deformity correction when compared to TGRs (Luhmann, Smith, et al. 2017; Luhmann & McCarthy 2017; Andras et al. 2015).

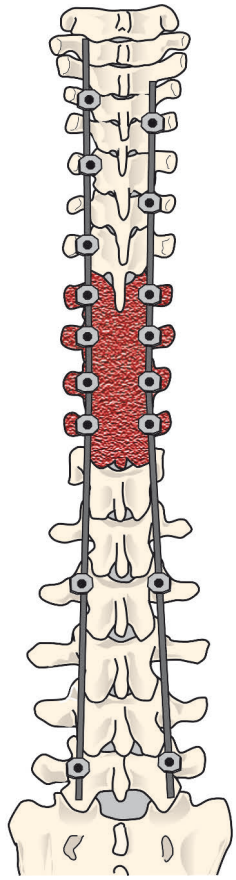

Figure 5. Passive Shilla instrumentation. Illustration adapted from Medtronic Inc.

Curve migration during the treatment with Shilla instrumentation is common (Wilkinson et al. 2019). However, the long-term result of the migration is unknown. Typical complications along with the progression of the deformity include rod fractures, wound infections, and screw pull-out (McCarthy et al. 2015). A study on the cost-effectiveness showed Shilla growth guidance to compare favorably to TGRs and MCGRs (Luhmann et al. 2018).

2.5 Pulmonary outcomes of growth-friendly treatment

There is limited evidence on the effect of growth-friendly implants on the respiratory function. Due to the young age and possible co-morbidities, the measurement of pulmonary function is often complicated (Vogt et al. 2014). Spirometry requires high patient co-operation, which complicates spirometry in very young or disabled

patients. Arm span and body weight can be used when assessing pulmonary function (Dimeglio et al. 2012). Arm span correlates with thoracic function parameters when height is complicated due to the deformity. Complicated breathing increases caloric consumption, which may lead to low body weight (Redding 2014). Chronic hypoxemia may increase hemoglobin, which may resolve with improvement of the pulmonary function (Barrett et al. 2016). Epilepsy, scoliosis not related to cerebral palsy, and a major scoliosis over 70 degrees increases the long-term risk for pneumonia (Keskinen et al. 2015).

Yoon et al. reported a 14% improvement in the forced vital capacity with treatment with MCGRs (Yoon et al. 2014). Improvement of the spinal deformity does not seem to correlate with improvement of fast vital capacity (Redding et al. 2011).

2.6 Quality of life, psychological burden

Chronic illnesses during the childhood greatly affect the quality of life of the patients and their families (Corona et al. 2011; Lauder et al. 2018). EOS is linked to an elevated incidence of depression and anxiety (Aslan et al. 2017). Repetitive surgical treatment further adds to the psychological burdens (Flynn et al. 2012). Deformity correction does not seem to affect the health-related quality of life (Hell et al. 2019). A study of 610 patients with early onset scoliosis concluded the etiology as the main influencer of the quality of life, with patients with neuromuscular or syndromic EOS linked to lower HRQoL scores (Ramo et al. 2021).

Several health-related outcome scores may be used to assess quality of life in patients with early onset scoliosis. These may be described as general health scores, anatomy-specific scores, and disease-specific scores.

A disease-specific instrument, the Early Onset Scoliosis Questionnaire 24 (EOSQ-24) has been developed to assess the quality of life in patients with EOS (Corona et al. 2011; Matsumoto et al. 2014). It consists of 24 domains: general health, pain or discomfort, pulmonary function, transfer, physical function, daily living, fatigue or energy level, emotion, parental burden, financial burden, child satisfaction, and parental satisfaction. The EOSQ-24 can be answered by both the patient and caregivers. Studies have shown the EOSQ-24 to be valid, reliable, and responsive in patients with EOS (Matsumoto et al. 2018). The Finnish translation of the EOSQ-24 is yet to be validated.

The Scoliosis Research Society 24-item questionnaire (SRS-24) was originally developed to assess the quality of life in patients with adolescent idiopathic scoliosis (Haher et al. 1999). It consists of 24 questions divided to seven domains: pain, general self-image, postoperative self-image, general function, overall level of activity, postoperative function, and satisfaction. The SRS-24 may correlate with the

EOSQ-24 in patients with congenital EOS without developmental delays (Li et al. 2020). The Scoliosis Research Society score may not have optimal sensitivity in patients younger than 18 years (Parent et al. 2010).

The Spinal Appearance Questionnaire (SAQ) is a disease-specific patient reported outcome score for patients with adolescent idiopathic scoliosis (Sanders et al. 2007). It specifically measures the patient's and caregiver's perception of the appearance of the spinal deformity. However, the SAQ may not be optimal for young patients due to difficult questions and illustrations (Mulcahey et al. 2011).

3 Aims

The aim of this thesis was to study the outcomes of modern growth-friendly instrumentations in early onset scoliosis. We studied the outcomes using the rate of deformity correction, thoracic growth gain, the incidence of complications, and the effect of the treatment on the health-related quality of life.

1. To compare the outcomes of growth-friendly treatment with magnetically controlled growing rods (MCGRs) to traditional growing rods (TGRs) in patients with severe early onset scoliosis of at least 90°. We hypothesized that magnetically controlled growing rods would provide similar deformity correction and thoracic growth as compared to traditional growing rods with fewer complications.
2. To compare the outcomes of the passive Shilla growth guidance system to MCGRs in patients with neuromuscular or syndromic early onset scoliosis. Our hypothesis was that the Shilla instrumentation would provide similar results in patients with neuromuscular or syndromic early onset scoliosis when compared to patients with similar background treated with magnetically controlled growing rods.
3. To compare the outcomes of growth-friendly treatment in patients with early onset scoliosis and skeletal dysplasia to patients with idiopathic early onset scoliosis. We hypothesized that the patients in the skeletal dysplasia group would have more complications, gain less thoracic height, and have lower health-related quality of life as compared to the idiopathic patients.

4 Materials and Methods

This study consists of retrospective reviews of a prospectively collected international database (Paediatric Spine Study Group, PSSG), and patient series from Turku University Hospital and Tampere University Hospital. The Paediatric Spine Study Group is an international database with 72 institutions in 12 countries. Study permits were applied from University of Turku, University of Tampere, and PSSG. All manuscripts were accepted by the co-authors before submitting to the journals.

Table 3. Clinical characteristics of the studies.

	study i		**study ii**		**study iii**	
	MCGR	TGR	MCGR	Shilla	Skeletal dysplasia	Idiopathic
Number of patients	44	44	18	13	33	33
Age at surgery	7.40 (2.4–10)	7.01 (2.5–10)	6.8 (2.1–10)	6.0 (2.7–9.1)	5.3 (1.5–10.1)	5.4 (1.8–9.6)
Female sex	34 (77%)	30 (68%)	7 (39%)	5 (38%)	21 (64%)	20 (61%)
Follow-up time	2.0	2.0	4.0 (2.0–9)	3.2 (1.3–6.8)	5.6 (1.5–13)	7.1 (2.1–16)
Type of EOS						
congenital	5 (11%)	5 (11%)	0	0	0	0
neuromuscular	25 (57%)	25 (57%)	11 (85%)	12 (56%)	0	0
syndromic	8 (18%)	8 (18%)	2 (15%)	6 (30%)	33 (100%)	0
idiopathic	6 (14%)	6 (14%)	0	0	0	33 (100%)

EOS, early onset scoliosis; MCGR, magnetically controlled growing rod; TGR, traditional growing rod; Shilla, Shilla passive growth guidance.

4.1.1 Study I

Study I was performed as a retrospective review of a prospectively collected PSSG database. Patients who were treated with MCGRs for severe EOS over 90 degrees were identified from the database. These patients were matched using etiology, age, and gender with patients treated with TGRs. Inclusion criteria were age of 10 years or less, EOS deformity over 90 degrees, minimum of two years of follow-up, and primary intervention with MCGRs or TGRs. No first generation MCGRs were included. Patients in the MCGR group were treated during 2014–2018. Patients in the TGR group were treated during 2006–2017.

There were six idiopathic, 25 neuromuscular, eight syndromic, and five congenital EOS in both groups. Of the neuromuscular patients, 15 in the MCGR group and 11 in the TGR group had cerebral palsy. Other neuromuscular diagnoses included: seven patients in the MCGR group and eight in the TGR group with spinal muscular atrophy, two patients in the MCGR group with myelomeningocele, one patient in the MCGR group and six in the TGR group with unspecified neuromuscular scoliosis, one patient with Ehlers-Danlos in the MCGR group, one patient with achondroplasia in the MCGR group, two patients with arthrogryposis in the MCGR group, one patient with Prader-Willi in both groups, one patient with Marfan in the TGR group, one patient with DiGeorge in the TGR group, three patients in the MCGR group and five in the TGR group with chromosomal anomality.

Four non-ambulatory patients in the MCGR group and three in the TGR group had pelvic fixation. Four patients in the MCGR group and eight in the TGR group had single rod constructs. We reported interim outcomes after 2 years of follow-up. None of the patients neither underwent final fusion nor completed all planned lengthenings. The mean age was 7.4 years (range, 2.4–10) in the MCGR group and 7.0 years (range, 2.5–10) in the TGR group. Of these patients with severe EOS, 61% were ambulatory in the MCGR group and 59% in the TGR group. There was a mean of 0.20 surgical procedures (range, 0–3) in the MCGR group and 3.2 (range, 0–6) in the TGR group. There was a mean of 5.9 lengthenings (range, 3–15) in the MCGR group and 3.7 (range, 3–5) in the TGR group.

4.1.2 Study II

Patients were collected from Turku University Hospital and Tampere University Hospital. The study was a consecutive series of patients with neuromuscular or syndromic EOS treated with MCGRs or Shilla instrumentation between 2010–2018. Inclusion criteria were age 10 years or less, major curve of at least 45 degrees, and initial treatment with MCGR or Shilla instrumentation. All patients had a body weight of at least 15 kilograms. No first generation MCGRs were used.

In total, 13 patients treated with Shilla and 18 patients treated with MCGRs met the inclusion criteria. In the Shilla group, 11 patients had neuromuscular and two syndromic EOS. In the MCGR group, 12 patients had neuromuscular and six syndromic EOS. In the Shilla group, neuromuscular diagnoses were as follows: six patients with spinal muscle atrophy type II, one with myelomeningocele, one with multiple developmental disability, one with progressive central nervous disease, and one with a developmental disability. There were two patients with syndromic EOS in the Shilla group: one patient with Edwards syndrome and one with arthrogryposis. In the MCGR group, the neuromuscular diagnoses were as follows: five patients with unspecified developmental disabilities, one with spinal muscle atrophy type II, and one with congenital muscular dystrophy. Six patients had syndromic EOS in the MCGR group: two patients had neurofibromatosis I, two had Marfan syndromes, one had Coffyn-Lowry syndrome, and one had Prader-Willi syndrome. The mean age was 6.0 years (range, 2.7–9.1) in the Shilla group and 6.8 years (range, 2.1–10) in the MCGR group. The mean follow-up time was 4.0 years (range, 2.0–9) in the Shilla group and 3.2 years (range, 1.3–6.8) in the MCGR group. There was a mean total of 1.5 (range, 1–3) surgical procedures in the Shilla group and 2.8 (range, 1–10) in the MCGR group. Shilla instrumentation requires no additional surgical lengthenings. In the MCGR group, there was a mean of 7.4 lengthenings (range, 2–15). Four patients in the Shilla group and five in the MCGR group underwent final fusion.

4.1.3 Study III

Study III was performed as a retrospective review of the PSSG database. In this study, patients with skeletal dysplasia treated with growth-friendly surgical instrumentation for EOS were identified. These patients were then matched with idiopathic patients using age, type of index surgery, and number of the lengthening procedures. Inclusion criteria were age 10 years or less, major curve of at least 30 degrees, minimum of two years of follow-up, and minimum of three lengthenings. Patients were treated between 1997–2016.

In the skeletal dysplasia group, seven patients had osteogenesis imperfecta, six had diastrophic dysplasia, four had camptomelic dysplasia, three had spondyloepiphyseal dysplasia, three had achondroplasia, two had cleidocranial dysplasia, two had atelosteogenesis type III, one had chondrodysplasia punctate, and one had bent bone dysplasia. Four children had an unknown skeletal dysplasia. The mean age was 5.3 years (range, 1.5–10.1) in the SD group and 5.4 years (range, 1.8–9.6) in the idiopathic group. The mean follow-up time was 5.6 years (range, 1.5–13) in the SD group and 7.1 years (range, 2.1–16) in the idiopathic group. Mean preoperative height and weight were significantly lower in the SD group. Patients

were matched with the primary surgical method: TGR was used in 13 patients, VEPTR in 13 patients, and MCGR in seven patients in both groups. There was an average of 7.2 (range, 3–19) surgical procedures in the SD group and 8.2 (range, 3–22) procedures in the idiopathic group. In the SD group, there was an average of 8.5 lengthenings (range, 2–21) as compared to 9.5 lengthenings (range, 4–23) in the idiopathic group. Nine patients in the SD group and 16 patients in the idiopathic group underwent final fusion.

4.2 Statistical analysis

Chi-squared test was used for categorical parameters. For continuous parameters, independent sample t-tests were used. Implant survival was analyzed in study I using the Kaplan-Meier curve. EOSQ-24 scores were analyzed between the groups using Mann-Whitney U tests. Wilcoxon's ranked tests were used to compare preoperative and postoperative EOSQ-24 scores. P-values under 0.05 were considered statistically significant. Analyses were performed with R (R Core Team, R 4.1.1) in studies I and II and with JMP Pro (JMP®, Version 14 SAS Institute Inc., Cary, NC, 1989–2021) in study III.

4.3 Ethical approval

Institutional Review Board approval and ethical committee approval were obtained from the Turku University Hospital, Turku, Finland, and Tampere University Hospital, Tampere, Finland. Informed consent was obtained from the patients treated in our institution that were contacted. Study permits were received from the Pediatric Spine Study group for studies I and III.

5 Results

5.1 Magnetically controlled growing rods compared to traditional growing rods in severe early onset scoliosis (Study I)

Forty-four patients treated with MCGRs for severe early onset scoliosis of at least 90 degrees were identified from the PSSG database. These patients were matched with patients treated with TGRs using the type of the scoliosis (congenital, neuromuscular, syndromic, idiopathic), age, and sex. The patient baseline characteristics were similar between the groups (Table 4). The mean age at surgery was 7.4 years in the MCGR group and 7.0 years in the TGR group (p=0.149). The matching with type of the scoliosis and age was successful. However, in the MCGR group, 34 (77%) of the patients were female, as compared with 30 (68%) in the TGR group (p=0.338). The mean preoperative major curves were 104° (range, 90°–130°) in the MCGR and 104° (90°–139°) in the TGR group (p=0.472). Dual rod system was used in 90% in the MCGR and 82% in the TGR group (p=0.214). Two patients in the TGR group had preoperative halo traction.

Table 4. Clinical characteristics of the groups in study I.

	MCGR	TGR	Significance
Age at surgery	7.40 (2.4–10)	7.01 (2.5–10)	0.149
Female gender	34 (77%)	30 (68%)	0.338
Mean preoperative height, cm, (range)	111 (82–133)	111 (81–152)	0.498
Mean preoperative weight, kg, (range)	19.3 (9.4–41)	19.5 (11–49)	0.472
Classification			
Congenital	5	5	1
Neuromuscular	25	25	1
Syndromic	8	8	1
Idiopathic	6	6	1
Mean number of lengthenings	5.9 (3–15)	3.7 (3–5)	<0.001
Mean number of surgical procedures	0.20 (0–3)	3.2 (0–6)	<0.001
Final fusion	4 (9%)	25 (57%)	<0.001

MCGR, magnetically controlled growing rod; TGR, traditional growing rod.

Radiographic outcomes are presented in Table 5. Mean major curve after the initial surgery was 53° (21–85) in the MCGR group and 57° (20–104) in the TGR group (p=161). At the 2-year follow-up, the major curve was 52° (range, 22–98) in the MCGR group and 66° (range, 31–103) in the TGR group (p=0.001). During the follow-up period, the annual thoracic height increase was 10 mm in the MCGR group and 11 mm in the TGR group (p=0.388). Minimum thoracic height of 18 cm was reached in 28 patients in the MCGR group and 26 in the TGR group (relative risk 1.08, 95% confidence interval 0.773–1.501, p=0.827).

Table 5. Radiographical outcomes of the groups in study I.

	MCGR	TGR	P-value
Major curve (°) mean, (range)			
Pre-op	104 (90–130)	104 (90–139)	0.472
Post-op	53 (21–85)	57 (20–104)	0.161
2-year follow-up	52 (22–98)	66 (31–103)	0.001
Spinal height (T1-S1) mm, (range)			
Pre-op	240 (178–313)	233 (137–301)	0.197
Post-op	291 (238–350)	281 (204–365)	0.096
2-year follow-up	315 (241–391)	303 (223–425)	0.132
Thoracic height (T1-T12) mm, (range)			
Pre-op	155 (108–202)	152 (99–210)	0.336
Post-op	184 (141–260)	177 (118–233)	0.113
2-year follow-up	202 (149–280)	192 (129–256)	0.088
Thoracic kyphosis (°) mean, (range)			
Pre-op	63 (19–104)	61 (0–99)	0.365
Post-op	35 (9–66)	43 (13–87)	0.022
2-year follow-up	45 (25–71)	54 (28–81)	0.010

The quality of life was assessed using the EOSQ-24 questionnaire preoperatively and at the 2-year follow-up. All patients in the MCGR group had EOSQ-24, while only 17 patients in the TGR group had preoperative EOSQ-24 data. The patients in the TGR group with EOSQ-24 data were matched with MCGR patients (Table 6). Pulmonary function domain in the mean EOSQ-24 scores was significantly better in the MCGR group. There were no significant differences in other domains.

Table 6. EOSQ-24 scores in study I.

	Pre-op			2-year follow-up		
	MCGR	TGR	P-value	MCGR	TGR	P-value
General health	72.7	71.4	0.966	75.0	60.0	0.064
Pain/discomfort	67.2	65.4	0.857	69.2	64.2	0.656
Pulmonary function	68.8	74.0	0.770	93.4	80.8	0.036
Transfer	62.5	71.4	0.576	58.3	63.3	0.714
Physical function	52.6	50.9	0.983	58.3	57.8	0.950
Daily living	38.3	41.3	0.709	55.8	37.5	0.166
Fatigue/energy level	67.2	60.7	0.419	65.8	58.3	0.487
Emotion	70.3	64.2	0.701	80.0	64.4	0.089
Parental impact	64.3	60.4	0.759	72.5	59.3	0.274
Financial impact	67.9	57.1	0.252	76.8	58.9	0.142
Child satisfaction	66.1	58.9	0.607	69.6	65.4	0.649
Parent satisfaction	61.2	55.4	0.586	66.7	62.5	0.601

There was a total of 10 complications in the MCGR group as compared with 26 in the TGR group during the 2-year follow-up period (p=0.019, Table 7). In the MCGR group, seven patients had at least one complication as compared with 17 in the TGR group (p=0.008). There were significantly more rod fractures and deep surgical infections in the TGR group. The incidence of complications requiring revision surgery was analyzed with the Kaplan-Meier curve. There were significantly more complications requiring revision surgery in the TGR group (p<0.001, Figure 6).

Table 7. Complications in study I.

	MCGR	TGR	P-value
Total number of complications, (range)	10 (0–3)	26 (0–4)	0.019
At least one complication, (%)	7 (16%)	17 (39%)	0.008
Unplanned revisions, (range)	9 (0–3)	22 (0–4)	0.002
Deep surgical site infection, (range)	1 (0–1)	11 (0–4)	0.001
Implant failure, (range)	8 (0–3)	11 (0–3)	0.221
Anchor failure, (Range)	3 (0–1)	3 (0–1)	0.500
Rod fracture, (Range)	2 (0–2)	7 (0–3)	0.040
Failure to lengthen, (Range)	1 (0–1)	0	0.160
Neurological complication, (Range)	1 (0–1)	2 (0–1)	0.328
Neuromonitoring change, (Range)	0	2 (0–1)	0.160
Neurological deficit, (Range)	0	0	0
Dural tear (Range)	1 (0–1)	0	0.160

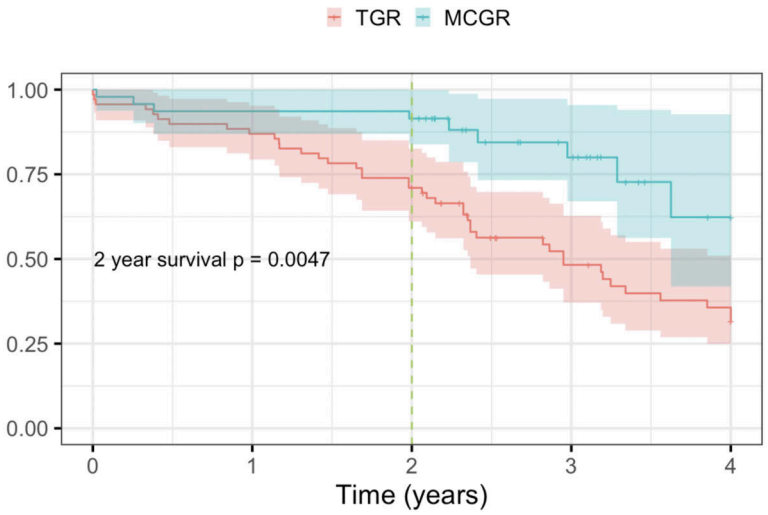

Figure 6. Complications requiring revision surgery analyzed with Kaplan-Meier survival curve. Figure from Saarinen 2021 JBJS with the permission from the journal.

5.2 Shilla growth guidance compared to the magnetically controlled growing rods in neuromuscular and syndromic early onset scoliosis (Study II)

Patients with syndromic or neuromuscular early onset scoliosis treated with Shilla instrumentation or MCGRs were identified from University of Turku and University of Tampere. The patient characteristics and the follow-up time were similar between the groups. There were 13 patients in the Shilla group and 18 patients in the MCGR group. Eleven patients in the Shilla group and 12 patients in the MCGR group had neuromuscular EOS. Neuromuscular etiologies were as follows in the Shilla group: six patients with spinal muscle atrophy type II, one patient each with myelomeningocele, multiple developmental disabilities, a progressive central nervous disease, and a developmental disability. Two patients in the Shilla group had syndromic EOS: one with Edwards syndrome, one with arthrogryposis. In the MCGR group, the neuromuscular etiologies were as follows: five had an unspecified developmental disability, one had spinal muscle atrophy type II, and one had congenital muscular dystrophy. Six had syndromic EOS in the MCGR group: two neurofibromatosis I, two Marfan syndromes, one Coffyn-Lowry syndrome, one Prader-Willi syndrome.

Table 8. Clinical characteristics of the groups in study II.

	Shilla	MCGR	Significance
Age at surgery	6.0 (2.7–9.1)	6.8 (2.1–10)	0.164
Female gender	5 (38%)	7 (39%)	0.981
Mean follow-up	4.0 (2.0–9)	3.2 (1.3–6.8)	0.093
Classification			
Neuromuscular	11	12	1.0
Syndromic	2	6	1.0
Mean number of lengthenings	None	7.4 (2–15)	
Mean number of surgical procedures	1.5 (1–3)	2.8 (1–10)	0.036
Final fusion	4 (31%)	5 (28%)	0.856

Shilla, Shilla passive growth guidance; MCGR, magnetically controlled growing rod.

The preoperative major curve was 64° (39–108) in the Shilla group and 58° (45–85) in the MCGR group (p=0.151). After the initial surgery, the major curves were 22° (6.7–52) in the Shilla group and 28° (9.8–46) in the MCGR group (p=0.095, Table 9). At the last pre-definitive visit, the major curves were 31° (9.4–54) in the Shilla group and 30° (16–53) in the MCGR group. The mean correction was 45% in the Shilla group and 48% in the MCGR group (p=0.383).

Mean preoperative thoracic height was 165 mm in the Shilla group and 147 in the MCGR group. At the last pre-definitive visit, the mean thoracic heights were 207 mm and 200 mm, respectively. The mean annual increase in the thoracic height was 6.2 mm in the Shilla group and 11 mm in the MCGR group (p=0.019). The mean annual spinal height increase was 7.2 mm in the Shilla group and 15 mm in the MCGR group (p=0.004).

Table 9. Radiographic outcomes of the groups in study II.

Major Curve (°)	Shilla	MCGR	P-value
Pre-op	64 (39–108)	58 (45–85)	0.151
Post-op	22 (6.7–52)	28 (9.8–46)	0.095
Pre-definitive	31 (9.4–54)	30 (16–53)	0.392
Definitive	12 (0–21)	16 (5.1–32)	0.253
Spinal height (T1-S1, mm)			
Pre-op	272 (206–366)	245 (180–290)	0.022
Post-op	306 (251–372)	276 (236–319)	0.004
Pre-definitive	332 (290–406)	323 (282–388)	0.194
Definitive	386 (345–462)	349 (330–368)	0.117
Thoracic height (T1-T12, mm)			
Pre-op	165 (126–226)	147 (92–178)	0.024
Post-op	186 (152–235)	166 (138–190)	0.003
Pre-definitive	207 (168–256)	200 (165–248)	0.202
Definitive	254 (226–320)	220 (200–237)	0.107
Maximum thoracic kyphosis (°)			
Pre-op	45 (6.8–80)	39 (7.4–67)	0.249
Post-op	28 (12–53)	25 (3.8–45)	0.226
Pre-definitive	31 (13–54)	22 (3.0–38)	0.030
Definitive	22 (16–30)	14 (6.0–29)	0.117
Maximum lumbar lordosis (°)			
Pre-op	23 (3.5–48)	38 (-4.0–73)	0.026
Post-op	34 (15–48)	39 (1.4–52)	0.147
Pre-definitive	39 (9.8–54)	39 (9.9–60)	0.480
Definitive	43 (34–48)	49 (42–67)	0.197

Postoperative EOSQ-24 data at the end of the follow-up was available from nine patients in the Shilla group and 15 patients in the MCGR group (Table 10). There were no statistically significant differences in the EOSQ-24 domains between the groups. In both groups, highest scores in the EOSQ-24 were in the pulmonary function domain, while the lowest scores were in the daily living domain.

Table 10. EOSQ-24 scores in study II.

	Shilla (N = 9)	MCGR (N = 15)	P-value
General Health	71 (38–100)	69 (38–100)	0.928
Pain/Discomfort	74 (0–100)	72 (50–100)	0.533
Pulmonary Function	96 (88–100)	86 (50–100)	0.109
Transfer	57 (25–100)	57 (0–100)	0.908
Physical Function	42 (8.3–67)	66 (17–100)	0.095
Daily Living	23 (0–63)	48 (0–100)	0.186
Fatigue/Energy level	73 (38–100)	65 (13–100)	0.590
Emotion	71 (25–100)	76 (25–100)	0.641
Parental Impact	44 (5.0–60)	60 (25–100)	0.187
Financial Impact	61 (25–100)	70 (25–100)	0.562
Child Satisfaction	66 (50–100)	63 (25–100)	0.756
Parent Satisfaction	58 (25–100)	64 (0–100)	0.622

There was no significant difference in the incidence of complications between the groups (Table 11). Five patients in the Shilla group and six patients in the MCGR group had at least one complication during the treatment (p=0.768). The complications in the Shilla group included the following: rod perforated through skin leading to infection and revision with new instrumentation, anchor failure leading to worsening of balance and requiring revision surgery, broken and detached rod requiring revision surgery, detached rod requiring revision surgery, and postoperative pneumonia. The complications in the MCGR group were as follows: broken distractor mechanism leading to revision surgery and new instrumentation with TGR; worsened balance and anchor close to spinal cord requiring revision; anchor failure, resolved change in the intra-operative monitoring during revision surgery; reversible changes in the motor evoked potentials during the index operation; anchor and rib connector failure, rod detachment, rod stuck due to metallosis requiring revision, and postoperative pneumonia.

Four patients in the Shilla group and five in the MCGR group reached final fusion surgery at the end of the follow-up (p=0.856). The treatment continued for 4.5 years in the Shilla group and 3.7 years in the MCGR group before the final fusion (p=0.244). After the final fusion, the mean major curve was 12° (range, 0–21) in the Shilla group and 16° (range, 5.1–32) in the MCGR group (p=0.252). The mean thoracic height after the final fusion was 254 mm in the Shilla group and 220 mm in the MCGR group (p=0.107).

Table 11. Complications in study II.

Complication	Shilla	MCGR	P-value
Total number	5 (38%)	10 (56%)	0.347
Surgical	4 (31%)	8 (44%)	0.116
Mechanical	4 (31%)	8 (44%)	0.440
Neurological	0	1 (5.6%)	0.388
Deep wound infection	1 (7.7%)	0	0.232
Other	1 (7.7%)	2 (11%)	0.751
Revision surgery*	4 (31%)	4 (22%)	0.592

*Final fusion not included

5.3 Results of growth-friendly instrumentation in the treatment of early onset scoliosis in children with skeletal dysplasias (Study III)

In study III, growth-friendly treatment was compared between patients with skeletal dysplasia (SD) and patients with idiopathic early onset scoliosis. From the PSSG register, 33 children with skeletal dysplasia were identified. These patients were matched with idiopathic EOS patients using age, gender, type of index surgery, and number of lengthenings. The patient characteristics were similar between the groups (Table 12).

Table 12. Clinical characteristics of study III.

	Skeletal dysplasia	Idiopathic	Significance
Age at surgery	5.3 (1.5–10.1)	5.4 (1.8–9.6)	0.406
Female gender			
Mean follow-up	5.6 (1.5–13)	7.1 (2.1–16)	0.046
Mean preoperative height, cm, (range)	96 (61–119)	109 (71–146)	<0.001
Mean preoperative weight, kg, (range)	15 (6.4–26)	20 (7.8–59)	0.028
Mean number of lengthenings	7.2 (3–19)	8.2 (3–22)	0.187
Mean number of surgical procedures	8.5 (2–21)	9.5 (4–23)	0.180
Final fusion	9 (27%)	16 (48%)	0.076

The mean major curve was 76° (range, 34–115) in the SD group and 75° (range, 51–113) in the idiopathic group (p=0.547, Table 13). After the initial surgery, this was corrected to 47° (range, 19–82) in the SD group and 48° (range, 18–95) in the idiopathic group (p=0.442). At the final follow-up, the mean major curves were 49°

(range, 13–113) in the SD group and 46° (range, 12 –112) in the idiopathic group (p=0.683).

Table 13. Radiographic outcomes of study III.

	Skeletal dysplasiA	Idiopathic	p-value
Mean major curve, °			
Pre-op	76 (34–115)	75 (51–113)	0.547
Post-op	47 (19–82)	48 (18–95)	0.442
final follow-up	49 (13–113)	46 (12–112)	0.683
Mean spinal height (T1-S1), mm (range)			
Pre-op	220 (140–340)	250 (164–390)	0.006
Post-op	255 (160–337)	288 (173–430)	0.016
final follow-up	276 (182–385)	334 (205–472)	< 0.001
Mean thoracic height (T1-T12), mm (range)			
Pre-op	132 (72–207)	157 (115–242)	0.001
Post-op	154 (93–211)	177 (115–257)	0.005
final follow-up	168 (93–229)	201 (114–282)	0.001
Mean maximum thoracic kyphosis, ° (range)			
Pre-op	55 (0–94)	46 (0–102)	0.086
Post-op	42 (0–73)	35 (5.3–77)	0.093
final follow-up	56 (14–133)	45 (5.3–79)	0.045

Skeletal dysplasias lead to shortened stature and limited capability of growth. Mean preoperative spinal height was 220 mm (range, 140–340) in the SD group and 250 mm (range, 164–390) in the idiopathic group (p=0.006). At the last follow-up, the mean spinal height was 276 mm (range, 182–385) in the SD group and 334 mm (range, 205–472) in the idiopathic group (p<0.001). After the initial surgery, the mean thoracic height was 154 mm (range, 93–211) in the SD group and 177 mm (range, 115–257) in the idiopathic group (p=0.005). At the last follow-up, the mean thoracic height was 168 mm (range, 93–229) in the SD group and 201 mm (range, 114–282) in the idiopathic group (p=0.001). The mean annual increase in the spinal height was 3.8 mm (range, 0.30–22) in the SD group and 6.5 mm (range, 0.50–29) in the idiopathic group (p=0.040). In the SD group, the major curve correction was significantly better in patients treated with growing rods than in patients treated with VEPTR. There was no difference in thoracic height increase between the treatment methods in the SD group.

In the SD group, 25 (76%) children had at least one complication as compared to 22 (67%) children in the idiopathic group (p=0.415, Table 14). There was an average of 2.5 (range, 0–12) complications per patient in the SD group and 2.3 (range, 0–14) in the idiopathic group (p=0.620). Intraoperative neuromonitoring changes were significantly more common in the SD group (6/33 vs. 0/33, p=0.010).

Table 14. Complications in study III.

	Skeletal dysplasia	Idiopathic	p-value
Complications in group, n (%)	25 (76)	22 (67)	0.415
Number of complications, mean (range)	2.5 (0–12)	2.3 (0–14)	0.620
Complication requiring surgery, n (%)	18 (55)	20 (61)	0.618
Deep surgical site infection, n (%)	9 (27)	8 (24)	0.778
Hardware failure, n (%)	13 (39)	14 (42)	0.802
Anchor failure, n (%)	4 (12)	6 (18)	0.492
Rod fracture, n (%)	6 (18)	4 (12)	0.492
Neurological complication, n (%)	6 (18)	1 (3)	0.046
Neuromonitoring change	6 (18)	0 (0)	0.010
Neurological deficit	1 (3)	1 (3)	1.00
Dural tear, n (%)	1 (3)	0 (0)	0.314
Morbidity, n (%)	0 (0)	1 (3)	0.314

In the SD group, 29 patients had preoperative EOSQ-24 data. Of these patients, 24 had follow-up data. In the idiopathic group, 31 patients had preoperative and 27 had final follow-up data. Mean follow-up was 5.6 years in the SD group and 7.1 years in the idiopathic group (p=0.046). Patients in the SD group had significantly worse preoperative EOSQ-24 scores in the domains of physical function (mean 61 in the SD group as compared to mean 90 in the idiopathic group, p=0.0002), daily living (mean 46 in the SD group as compared to 83 in the idiopathic group, p=0.0001), financial impact (mean 63 in the SD group as compared to 85 in the idiopathic group, p=0.001), and parental satisfaction (mean 65 in the SD group as compared to 72 in the idiopathic group, p=0.368) (Table 15). At the final follow-up, financial impact (mean 65 in the SD group as compared to 82 in the idiopathic group, p=0.018) and child satisfaction (mean 61 in the SD group as compared to 75 in the idiopathic group, p=0.038) were worse in the SD group. The EOSQ-24 domains did not improve during the treatment. The physical function domain worsened during the treatment in the idiopathic group.

Table 15. EOSQ-24 scores in study III.

Domain	pre-op (range)		p-value	final follow-up (range)		p-value
	Skeletal dysplasia (n = 29)	Idiopathic (n =31)		Skeletal dysplasia (n = 24)	Idiopathic (n = 27)	
General health	71 (37.5–100)	75 (25–100)	0.339	72 (25–100)	74 (37.5–100)	0.890
Pain/discomfort	69 (25–100)	75 (50–100)	0.141	69 (37.5–100)	69 (37.5–100)	0.964
Pulmonary function	76 (12.5–100)	81 (37.5–100)	0.827	85 (25–100)	80 (37.5–100)	0.229
Transfer	65 (0–100)	79 (25–100)	0.294	65 (0–100)	78 (25–100)	0.202
Physical function	61 (0–100)	90 (41.7–100)	0.0002	70 (25–100)	77 (25–100)	0.294
Daily living	46 (0–100)	83 (12.5–100)	0.0001	56 (12.5–100)	72 (12.5–100)	0.056
Fatigue/energy level	61 (12.5–100)	73 (37.5–100)	0.091	67 (12.5–100)	68 (25–100)	0.992
Emotion	71 (37.5–100)	79 (37.5–100)	0.128	68 (25–100)	70 (25–100)	0.601
Parental impact	65 (10–100)	72 (35–100)	0.368	64 (25–100)	74 (35–100)	0.137
Financial impact	63 (0–100)	85 (25–100)	0.001	65 (0–100)	82 (0–100)	0.018
Child satisfaction	57 (0–100)	65 (0–100)	0.203	61 (25–100)	75 (0–100)	0.038
Parent satisfaction	60 (25–100)	73 (25–100)	0.044	67 (25–100)	68 (0–100)	0.746

6 Discussion

The surgical treatment of early onset scoliosis (EOS) aims for deformity correction and further growth of the spine. Historical treatment with spinal fusion effectively corrected the deformity but prevented spinal growth. Growth-friendly instrumentations have been developed to allow spinal growth during the treatment. Modern instrumentations effectively prevent thoracic insufficiency syndrome, with most patients reaching the satisfactory thoracic height of 18 cm and deformity correction. Traditional growing rods require surgical lengthening every six months. This is linked to a high incidence of wound-related complications and exposes patients to repetitive anesthesia. Over time, less invasive techniques such as magnetically controlled growing rods (MCGRs) have been developed.

The key to effective surgical growth-friendly treatment with minimum complications is delaying surgical treatment with conservative methods and selecting the appropriate surgical method depending on the etiology, age, and the degree of the deformity. EOS deformities over 45 degrees generally require surgical intervention. Delaying the surgical treatment with conservative methods decreases the incidence of complications (Bess et al. 2010). Progressive scoliosis usually worsens during the conservative treatment. The length of the optimal delay is not known. The rate to which the deformity can be allowed to progress during the conservative treatment depends on the etiology and possible co-morbidities. Scoliosis over 70° is an independent risk factor for pneumonia in patients with neuromuscular early onset scoliosis (Keskinen et al. 2015). In congenital early onset scoliosis, severe deformity further stiffens the thoracic cavity and spine. For this reason, earlier intervention is often required in congenital EOS. Minor deformities with idiopathic etiology can resolve with conservative treatment without surgical intervention. The recommended surgical method and fixation depends on patient age, size, ambulatory capacity, and etiology.

Complications such as infections and instrumentation failure are common in patients treated with surgical instrumentation for early onset scoliosis (Bess et al. 2010). Improvements in general care and surgical techniques have decreased the incidence of complications. Repetitive surgical lengthenings in treatment with TGRs lead to a high incidence of deep surgical infections. The decreased rate of surgical

procedures in treatment with MCGRs and Shilla instrumentation reduces deep wound infections. Growth-friendly instrumentations are prone to mechanical complications. Further development of surgical implants has decreased the rate of mechanical complications, but further research and development is still needed.

We hypothesized that the reduced need for surgical procedures would have a positive effect on the quality of life in treatment with MCGR or Shilla instrumentations. In study I, the pulmonary function domain of the EOSQ-24 questionnaire was significantly better in the MCGR group as compared to the traditional growing rod (TGR) group. There were no differences in the other domains between the groups. There were no significant differences between the groups in EOSQ-24 scores in patients treated with MCGR and Shilla instrumentation in study II. In study III, the EOSQ-24 scores were lower in the skeletal dysplasia group both before and after the treatment. We hypothesize that co-morbidity in patients with skeletal dysplasia group worsens the quality of life scores when compared to idiopathic patients. It is possible that our sample size was not large enough in these studies to detect potential differences in the quality of life scores between the groups. A previous study showed better initial postoperative EOSQ-24 scores in patients treated with MCGRs when compared to TGRs (Doany et al. 2018). However, the scores deteriorated during the distraction period. A study on patients who received conversion from TGRs to MCGRs showed better postoperative transfer and energy domains in the MCGR groups but no differences between the converts and the TGR and MCGR groups (Bauer et al. 2019).

Two recent studies showed the largest contributing factor to be the etiology of the scoliosis (Hell et al. 2019; Ramo et al. 2021). In study III, quality of life was lower in the skeletal dysplasia group, in which co-morbidities were more severe than in the idiopathic group. The EOSQ-24 includes the caregiver satisfaction domain, which helps assessing the quality of life in extremely disabled patients. Quality of life is an important part when evaluating the results of surgical treatment. In early onset scoliosis, the goal of the surgical treatment is to prevent thoracic insufficiency syndrome. Development of as normal as possible cardiopulmonary function and well corrected spinal deformity are important secondary outcome parameters after the patient-reported quality of life outcome measures. According to the literature, this requires a sufficiently long thoracic spine with scoliosis at least 50 degrees at skeletal majority (Johnston et al. 2021).

6.1 Magnetically controlled growing rods in severe early onset scoliosis

Severe deformities may complicate the insertion of surgical implants. While TGRs have been shown to be an effective method in severe EOS over 90 degrees, they are

linked to a significant incidence of complications (Helenius et al. 2018). Treatment of severe EOS with MCGRs has not been widely studied previously. In a case report, Cheung et al. described a 12-year-old girl with severe EOS of 109 degrees treated successfully with MCGRs (Cheung et al. 2014). This patient was treated with daily distractions for 2.5 months, after which final fusion was performed. Welborn et al. compared patients with severe EOS treated using MCGRs with and without preoperative halo traction (Welborn et al. 2019). At the final follow-up, patients with preoperative halo traction maintained better major curve correction.

MCGRs have a large actuator part which prevents contouring. This may complicate insertion on extremely severe deformities or small patients (Cheung et al. 2019). Our results in study I indicate that children with severe deformities over 90 degrees can effectively be treated with MCGRs. TGRs may be used when difficult anatomy prevents the installation of MCGR actuators.

A previous study reported a high incidence of complications in the treatment of severe EOS with TGRs (Helenius et al. 2018). Repetitive lengthening procedures resulted in deep wound infections in 17% of the patients with severe EOS. In study I, we compared the need for revision surgery in patients with severe EOS treated with MCGRs and TGRs. There were significantly fewer unplanned revision surgeries and deep wound infections in the MCGR group. According to our findings, MCGRs reduce the incidence of complications in patients with severe EOS. Delaying the initial surgical treatment with conservative methods may decrease complications in severe EOS (Fletcher et al. 2012).

Dual rods are considered as the gold standard in the surgical treatment of EOS. However, difficult anatomies may prevent the installation of two growing rods. In these patients, single rod constructs may be used. Single rods have a higher incidence of instrumentation-linked complications, such as rod fractures (Thakar et al. 2018).

Severe EOS leads to a lower HRQoL than a moderate deformity (Helenius et al. 2019). We hypothesize that the reduced need for anesthesia and operative visits with MCGR treatment is beneficial to the children and their caretakers, although this is not reflected in the EOSQ-24 scores.

6.2 Shilla growth guidance in neuromuscular and syndromic early onset scoliosis

In study II, we compared a passive Shilla guidance system to the MCGR instrumentation in children with neuromuscular or syndromic EOS. The study showed comparable results between the groups. Our findings of satisfactory deformity correction and spinal growth reflect those of previous studies (McCarthy et al. 2014; McCarthy et al. 2015). Andras et al. reported better deformity correction and spinal height increase but significantly more surgical procedures in patients

treated with TGR when compared to Shilla (Andras et al. 2015). In our study, the deformity correction and spinal growth were comparable between the groups. Although there were no differences in the EOSQ-24 scores between the groups, the quality of life in patients treated with Shilla instrumentation requires further research.

Apical fusion is performed during the installation of the Shilla instrumentation. Fixed fixation is performed in the fused apical segment. Unlike TGRs or MCGRs, Shilla instrumentation provides control of the apex of the deformity.

The passive nature of the Shilla instrumentation results in minimal follow-ups and out-patient clinical visits. However, due to the passive nature, Shilla instrumentation lacks the additional growth-inducing distraction force. Shilla may be useful for treating skinny patients, for whom MCGR instrumentation is too large. Shilla instrumentation should be considered for the treatment in patients with severe neuromuscular involvement who are typically non-ambulatory. In these patients, the additional benefit from more invasive MCGR or TGR treatment is uncertain.

6.3 Growth-friendly treatment in children with skeletal dysplasia

Skeletal dysplasias lead to small stature and abnormally small thoracic height. Due to the etiology, these patients have very limited growth potential. A previous study reported similar improvement in major curve and spinal growth between patients with and without skeletal dysplasias treated with growth-friendly instrumentation (White et al. 2018). According to our findings in study III, the additional benefit for the thoracic growth of growth-friendly treatment is not apparent in these patients. Long-lasting growth-friendly treatment burdens the family, exposes patients to complications, and requires repetitive procedures and outpatient clinical visits. Growing rod treatment resulted in better deformity correction than treatment with VEPTR.

Skeletal dysplasias decrease the quality of life (Vaara et al. 1999; Dahan-Oliel et al. 2016; Dhiman et al. 2016). In patients with osteogenesis imperfecta, the degree of deformity has a negative effect on the HRQoL (Dahan-Oliel et al. 2016). In study III, HRQoL scores remained constant during the treatment but were significantly worse in the skeletal dysplasia group. Patients who have early onset scoliosis and skeletal dysplasia may benefit from deformity correction with early spinal fusion, which also increases thoracic height. Preoperative bracing or casting could be used to delay the fusion. Spinal fusion with preceding conservative treatment might be the optimal treatment for patients with skeletal dysplasia and spinal deformity.

6.4 Strengths and limitations

The multicenter approach allowed us to gather relatively large samples of patients with operatively treated early onset scoliosis. Early onset scoliosis and underlying etiologies are rare, complicating the gathering of a single center patient series. However, an international multicenter patient series limits the variables that can be collected. Precise surgical methods or types of fixations may not be available. These variables may however have a significant impact on the results of the operative treatment of EOS and need further research. Due to the multicenter approach, we did not have precise information on the perioperative treatment. The majority of the patients in these studies had a follow-up time of at least two years. However, long-term results still need further research. Pulmonary function data was not available for these studies. Lung function was assessed only with patient- or caretaker-reported EOSQ-24 data. Further research with spirometry is needed. We did not have quality of life data assessed with the EOSQ-24 for all patients. Our sample size may have been too small to reliably demonstrate meaningful differences in the EOSQ-24 data between the groups.

6.5 Future perspectives

Growth-friendly treatment of early onset scoliosis has developed significantly during the last ten years. Still, a lot remains to be improved.

Implant development has decreased mechanical complications. This is perhaps most apparent in the MCGRs, in which the second-generation implants greatly decreased mechanical failures. Still, rod fractures and mechanical failures are prominent during growth-friendly treatment. The long-term effect of metallosis in the MCGRs needs to be studied.

There is lot to learn about patient selection in growth-friendly surgical treatment. In the future, further evidence should improve implant and foundation selection and thus decrease the rate of complications. Early onset scoliosis is often linked to co-morbidities, which may result in permanent non-ambulatory status or weak growth-potential. It may not be beneficial to expose these patients to the demanding growth-friendly treatment. Growth-potential and the benefit of growth-friendly treatment in different skeletal dysplasias could be further studied.

Novel surgical methods and implants to treat EOS are being developed (Vaudreuil et al. 2018; Toftgaard Skov et al. n.d.; Lemans et al. 2021). These new inventions may provide more treatment options in the future.

7 Conclusions

The conclusions of the studies are:

1. Magnetically controlled growing rods provide effective deformity correction and spinal growth with significantly fewer unplanned revision surgeries than traditional growing rods in severe early onset scoliosis over 90 degrees.
2. Treatment with passive Shilla growth guidance instrumentation leads to comparable deformity correction, spinal growth, and incidence of complications with fewer surgical procedures when compared to magnetically controlled growing rods in patients with neuromuscular or syndromic early onset scoliosis.
3. The effect on thoracic height increase of growth-friendly surgical treatment is modest in patients with skeletal dysplasia and early onset scoliosis when compared to idiopathic patients. Patients with skeletal dysplasia had more complications and lower health-related quality of life as compared to idiopathic patients.

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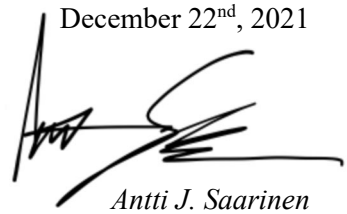

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