Spinal Deformity in Marfan Syndrome (MFS)

12

Nanjundappa S. Harshavardhana
and Mohammed H.H. Noordeen

Introduction

Marfan syndrome (MFS) was first described by the French physician Dr. Antonine Marfan in 1896 when he described a 5.5 year old girl named Gabrielle who had tall stature, long and slender limbs, with an asthenic build (dolichostenomelia) [1]. It is one of the most common inherited connective tissue disorders and is transmitted as an autosomal dominant trait characterised by complete penetrance, but with variable expressivity. The disorder is attributed to a mutation involving the Fibrillin (FBN-1) gene located on the long arm of chromosome 15 (i.e. 15q21) that shows striking pleotropism with clinical variability [2]. A family history of MFS with an affected first degree relative is usually present in 75 % of the instances. Up to 25 % of affected patients may not have a family history and they may represent a de novo mutation of FBN-1 [3]. The incidence of MFS is estimated to be 1–3 per 10,000 in the population and it affects both sexes equally often [4]. The diagnosis is largely clinical and is characterised by cardinal features that mainly affect three major systems, that is,

- The skeletal,
- The ocular, and
- The cardiovascular.

N.S. Harshavardhana, MS, Dip SICOT, EBOT (✉)
Department of Spinal Surgery, Spinal Deformity Unit (SDU),
Royal National Orthopaedic Hospital, Brockley Hill,
London, UK
e-mail: nharsha@outlook.com

M.H.H. Noordeen, MA, BM, MCh Ortho, FRCS(Tr&Orth)
Department of Trauma and Orthopaedic Surgery, Spinal Deformity Unit (SDU),
Royal National Orthopaedic Hospital, Brockley Hill,
London, UK
e-mail: hnoordeen@aol.com

A.H. Child (ed.), *Diagnosis and Management of Marfan Syndrome*,
DOI 10.1007/978-1-4471-5442-6_12

The genetic association was first established by Dietz et al. in 1991 when they detected a mutation of the FBN-1 gene. It shares overlapping clinical features with congenital contractural arachnodactyly (i.e. Beal's syndrome), which is caused by a mutation involving the FBN-2 gene [5]. In fact, it is believed that Dr. Marfan's original description of the affected girl indicates that she probably had this condition and would no longer meet the current diagnostic criteria of MFS. The differential diagnosis includes:

- Mitral valve prolapse syndrome,
- Weill-Marchesani syndrome,
- Loeys-Dietz syndrome,
- Shprintzen-Goldberg syndrome,
- Homocystinuria,
- Ehlers-Danlos syndrome,
- MASS (mitral, aortic, skin & skeletal) manifestation phenotype, and
- Beals syndrome.

Fibrillin-1 is an extracellular matrix glycoprotein that is essential for fibrinogenesis and is present in connective tissues, including bone. The mutations increase the susceptibility to proteolysis leading to the fragmentation of microfibrils, which causes changes in cell-to-cell signaling through the latent transfer binding protein. The abnormalities of fibrillin also cause a loss of inhibitory effect on transforming growth factor beta (TGF-β) which affects the microfibril structure systemically, resulting in the dysfunctional signaling of TGF-β that is implicated in the pathophysiology of MFS. Similarly increased TGF-β activation and signaling, secondary to mutations involving the TGFBR1 and TGFBR2 genes located on chromosomes 9 and 3, are also observed in patients with other Marfan-related disorders [6].

Children born with this condition are normal at birth with normal mentation, but the clinical manifestations become more evident with increasing age. The natural history is premature mortality, usually secondary to a cardiovascular event. Since the 1970s, with advances in cardiac sciences, surgeries focused on the aortic valvular area have significantly increased the longevity of these patients to near normal in contemporary era [7].

Diagnosis

MFS is characterised by cardinal skeletal features that include tall stature with thin habitus and long slender digits (arachnodactyly). The most common skeletal manifestation is scoliosis, which is seen in at least 60 % of the patients [8]. Chest cage deformities, i.e. pectus excavatum/ carinatum, are also common. They typically have arm span to height ratio of >1.05 with a decreased upper segment to lower segment (US:LS) ratio. Pes planus and protrusio acetabuli are also not uncommon.

The Ghent nosology has incorporated the clinical features of seven systems, and determines whether major/minor criteria and systemic involvement are present. The

major criteria are infrequent in other CTD and have high specificity. Nevertheless, debate persists to this day as to whether the Ghent nosology is too stringent and excludes truly affected MFS cases [9]. Further details of testing for MFS and the merits and limitations of these criteria are discussed in more detail in other chapters. The overall consensus, however, is to let the geneticist (rather than the clinician) apply the stringent Ghent nosology in the clinical diagnosis of MFS.

Scoliosis in MFS

The axial skeleton is the most commonly affected part of skeletal system in MFS. The reported incidence of scoliosis in established diagnosis of MFS varies from 40 to 60 % [10]. In 1939, the first reported series, published by Fahey et al., had 45 scoliosis patients from 132 MFS cases [11]. Subsequently, Sinclair et al. (1960), Wilner et al. (1964), and Scheier et al. (1967) observed scoliosis of mild to moderate severity [12–14]. Ford et al. (1968), in their review of MFS, found at least 13 % of patients had severe scoliosis which required aggressive bracing, fusion, or both [15]. Sliman et al. (1971) were the first to observe striking similarities and unique differences between the scoliosis of MFS vs. idiopathic etiology, and they concluded that MFS scoliosis has a poorer prognosis [16]. Robins et al. (1975) reported a 44 % incidence of scoliosis (35 out of 64 MFS patients with scoliosis) and observed poor response to treatment with a Milwaukee brace (MB) [17]. Spinal fusion with Harrington instrumentation yielded a 41 % correction with an average loss of 7° over 2.3 years of follow-up [17]. Sponseller et al evaluated 113 patients with MFS from their hospital database and found that 82 of them were skeletally immature. 52 out of 82 patients had scoliosis, and all but two (i.e. 50 out of 82) had scoliosis which was convex to the right [18]. The incidence of scoliosis in their series was 60 %. The thoracic spine was the most common region affected, followed by the thoracolumbar junction. Though these curves resembled the idiopathic curve type/pattern, certain unique features were evident. MFS patients had a higher incidence of having double thoracic or triple major curves. In addition, on the sagittal plane, there was a loss of thoracic kyphosis (TK) with reversal to thoracic lordosis in the most severe cases [18]. This, coupled with pectus excavatum, resulted in a reduced AP diameter of the chest with resultant mechanical compression of the large airways, which predisposed these patients to recurrent chest infections. Fewer patients had hyperkyphosis (i.e. TK of >50°) which was seen in 40 %.

The scoliosis in MFS differs significantly from idiopathic scoliosis by having rapid progression with a poor response to non-operative treatment. Furthermore, vertebral morphology is affected significantly, which makes operative treatment challenging. The key findings in vertebral bodies and posterior elements in children with MFS scoliosis include [19]:

- Narrow pedicles,
- Vertebral and sacral scalloping,
- Wide transverse processes,

- Thin laminae, and
- Low bone mineral density (BMD).

There is a high prevalence of lumbosacral transitional vertebra, and the presence of spondylolysis/spondylolisthesis is also not uncommon. Sponseller et al studied the sagittal plane deformity in MFS and proposed a classification to describe it. The two main sub-groups identified were (i) Transitional vertebra at or above L2, and (ii) Transitional vertebra below L2. Further sub-types for these two main sub-groups are illustrated in Table 12.1 [18]. They emphasised evaluating the sagittal profile in choosing fusion levels for scoliosis correction to avoid junctional problems (i.e. proximal junctional kyphosis [PJK] and distal junctional kyphosis [DJK]).

Table 12.1 The Sagittal profile classification in Marfan syndrome [21]

Type I	Normal transitional zone (at or above L2)	Normal kyphosis (20°–50°)	
		Hypokyphosis (≤19°)	
		Hyperkyphosis (≥51°)	
Type II	Abnormal transitional zone (below L2)	Long kyphosis	
		Reversal of direction	

Multi-planar deformities (i.e. kyphoscoliosis) with chest cage deformation secondary to pectus excavatum/carinatum pose unique challenges and are often fraught with life-threatening risks. Multi-disciplinary input with the involvement of a cardiologist, respiratory physician, paediatrician, thoracic surgeon, in addition to a spinal surgical team is desired to optimise surgical results and outcomes.

Increasingly, medical rapid prototyping technology (RPT) based on three-dimensional printing principles is used to replicate 1:1 scale models, which helps to better illustrate the underlying deformity, counsel patients and parents, and plan the surgical correction prior to intraoperative correction [20]. Evidence exists which confirms this to be a standard of care in complex spinal deformity vertebral column resection (VCR) surgeries [21]. One such case example of an RP model in a patient with complex multi-planar congenital spinal deformity along with its three-dimensional computed tomography reconstruction (i.e. 3D CT) scan is illustrated in Fig. 12.1.

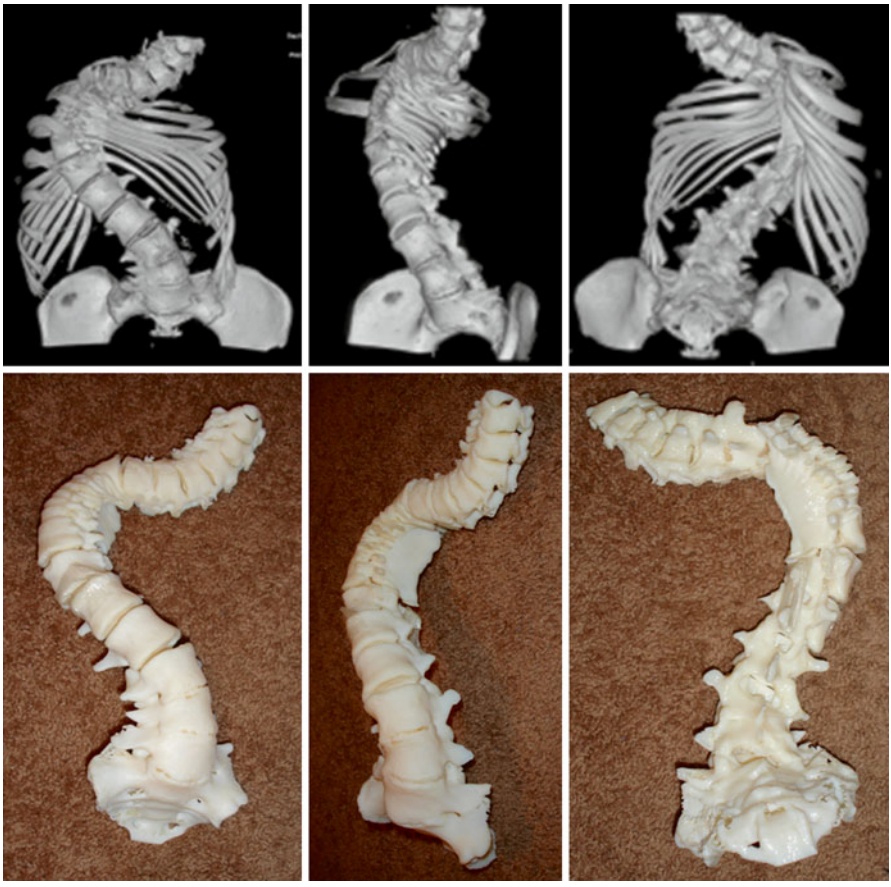

Fig. 12.1 Illustrative case example of a rapid prototyping (RP) model of a severe congenital multi-planar spinal deformity with 3D-CT reconstruction images

The appendicular skeleton is also involved, producing leg length inequality (LLE), angular deformities of the lower extremities, pes planus, and flexion contracture at the elbows. Protrusio acetabuli was also found to be common [22] (See the rheumatological manifestations of MFS and the surgical management of pectus excavatum/carinatum in other chapters of this book).

Cervical Spine

Patients with MFS have a loss of normal cervical lordosis or reversal of lordosis with cervical kyphosis on sagittal evaluation. The incidence of cervical kyphosis was 16 % (i.e. one in six) and at least 36 % of the patients had basilar impression (i.e. cranial setting) [23]. In addition, they also have increased atlanto-axial movement on flexion-extension movement, particularly in children, who are at a risk of developing atlanto-axial rotatory subluxation in up to 20 % of the instances. Ligamentous laxity with some degree of muscle hypotonia is believed to be the causative factor behind these manifestations. Surprisingly, the incidence of cervical stenosis was rare and no more than 2–3 % [23]. The incidence of neck pain was similar to age- and sex-matched controls without MFS. The overall risk of neurological complication in MFS is rare, and routine screening radiographs of the neck in all patients with MFS, prior to a general anaesthetic, is not recommended. Patients with MFS ought to refrain from playing contact sports (to protect the aorta and the lens of the eye) and any sports that cause high impact loading of the cervical spine (in particular, diving, weight lifting, and American football) [23].

Dural Ectasia

Dural ectasia (DE) refers to the widening of the thecal sac and nerve root sleeves in the caudal portion of the spine. There is a high incidence of DE in MFS (56–92 %) and DE is not necessarily pathognomic of MFS [24]. Other conditions where it is commonly present include neurofibromatosis, Ehlers-Danlos syndrome, tumors, trauma, congenital scoliosis, and ankylosing spondylitis. In fact DE is the second most common manifestation of MFS after aortic dilation/dissection. The Ghent nosology recommends screening for DE, indicating its presence as high in importance for the diagnosis of MFS. CT and MRI scans detect DE with high sensitivity and specificity. The receiver operator characteristics (ROC) curve demonstrates a large area for both CT (0.863) and MRI (0.910), with the MRI being superior in addition to the added advantage of eliminating irradiation [25]. An index case example of MFS with dural ectasia as seen on T_2 weighted coronal and sagittal MRI images is illustrated in Fig. 12.2. One of the most widely used criteria for describing DE in MFS is the one proposed by Ahn et al., and it is summarised in Table 12.2. It comprises major and minor criteria and they recommended a volumetric *gold*

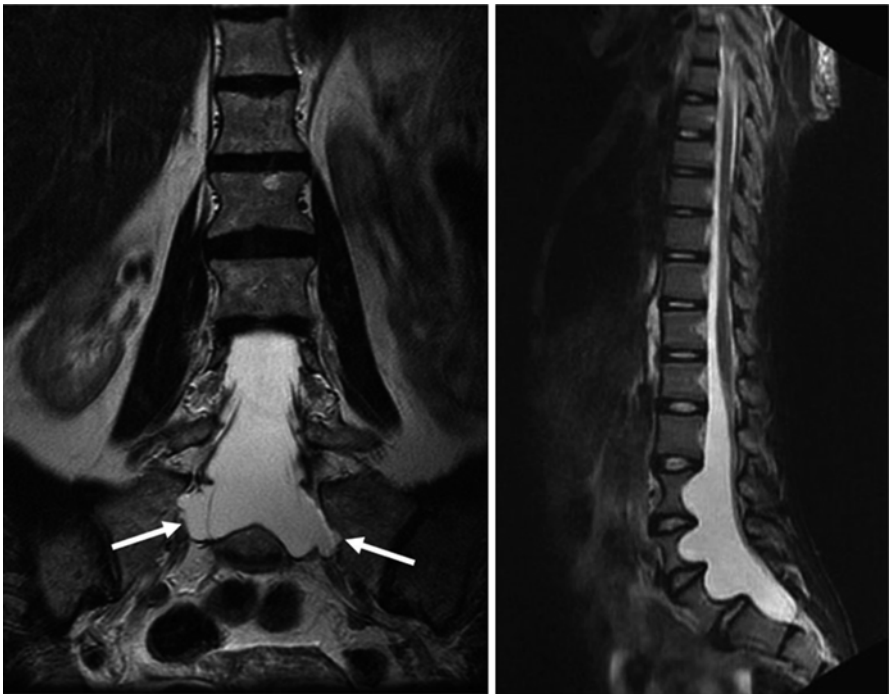

Fig. 12.2 A T_2 weighted MRI scan of the lumbar spine showing dural ectasia in a patient with Marfan syndrome. The lateral extensions of dura around the S_1 nerve root sleeves are indicated in *white arrows*

Table 12.2 The Ahn criteria for the description of dural ectasia in Marfan syndrome [28]

Major criteria	Minor criteria
1. Width of dural sac below L5 > width above L4 2. Anterior sacral meningocoele	1. L5 nerve root sleeve diameter >6.5 mm 2. S1 scalloping >3.5 mm

Dural ectasia exists if one major or two minor criteria are present

standard criteria for the diagnosis of DE to be a volume of >7 cm^3 (i.e. more than two standard deviations [SD] above the mean for normal controls) when measured from the caudal to inferior end plate of the L_5 vertebra [25].

DE develops owing to hydrostatic pressure exerted upon inherently weakened dura and it is invariably present below L_5 owing to this vertebra having the greatest fluid pressure in the most caudal portion of the spine. Its incidence increases as the patient ages [26]. DE most commonly causes intractable back pain or severe headaches, and neurological deficit necessitating decompression surgery. Patients can also be completely asymptomatic, and incidentally detected DE on advanced imaging can be seen in up to 40 % of MFS children. The natural history of DE is unknown and a diagnostic criterion to aid in the evaluation of DE in children is yet to be developed.

Spondylolisthesis

Patients with MFS have twice the incidence of spondylolisthesis compared to the general population (5–6 % vs. 2–3 %) [27]. The spondylolisthesis of MFS tend to be of an usually higher Myereding grade, with at least twice the slip angle (i.e. 30 %), in comparison to normal cohorts (whose average slip angle is 15 %). The slip angle further increased to an average of 60 % with the presence of scoliosis. Patients with bilateral pars defects had a high risk of progression owing to the vertebral body and sacral scalloping with DE. Symptomatic spondylolisthesis mandates the extension of instrumentation/inclusion of the pelvis in spinal fusion, which is fraught with complications such as pseudoarthrosis, dural leak, risk of arachnoiditis, and pseudomeningocoele. To this day, there is no published case series that has reported the surgical results of spondylolisthesis in MFS. Winter (1982) and Taylor (1987) have published case reports recommending either decompression with in-situ postero-lateral fusion or decompression with reduction and circumferential 360° fusion as treatment strategies [28, 29].

Bone Mineral Density (BMD) and Protrusio Acetabuli

There is a component of low BMD, especially in adult males with MFS who had an average T score of −1.54 (osteopenia) [30]. The BMD in adolescents and females was surprisingly found to be within normal limits, for reasons unknown, in a series of 51 patients (30 adults and 21 children) studied by Giampietro et al. [30]. Further evidence is needed to define the role of anti-osteoporotic medications (bisphosphonates, selective estrogen receptor modulators [SERM], etc) before their routine prescription for MFS. The incidence of protrusio acetabuli in MFS was reported to be at least 30 % and was independent of BMD of the hip and pelvis [31]. Protrusio acetabuli was purely a radiographic finding that did not correlate with the clinical symptoms and its presence alone was not felt to be an indication to either justify or recommend surgery.

Treatment of Scoliosis in MFS

The scoliosis of MFS closely resembles that of idiopathic scoliosis and the management in this chapter is therefore discussed along those lines. As in idiopathic scoliosis, management is covered under the following three sub-groups depending on age at the manifestation of scoliosis [32]:

(i) Infantile: from birth up to 3 years
(ii) Juvenile: between 3.1 and 9.9 years
(iii) Adolescent/Adult scoliosis: age ≥10 years.

Some professionals group the infantile/juvenile forms as one single entity and discuss them under the broad category ‘early-onset scoliosis’ (EOS), which is the

manifestation of spinal deformity in children aged ≤9.9 years [33]. The treatment of scoliosis in this chapter is therefore covered under two broad sub-groups, namely, (1) Early-onset scoliosis, and (2) Adolescent/adult scoliosis, with an emphasis on its surgical management with practical operative tips.

Early-Onset Scoliosis (EOS) in MFS (Infantile and Juvenile Sub-types)

Infantile scoliosis is the most severe form of MFS and almost all patients have an affected first degree relative diagnosed with MFS. It presents with severe deformity and often a kyphoscoliosis that progressed rapidly. In a series of 14 MFS patients with infantile scoliosis, Sponseller et al observed 13 of them had a family history of MFS [34]. The authors studied eight boys and six girls and observed that all had motor developmental delay. Longevity was significantly reduced, with mean survival of 13 years, and four patients died due to cardiac problems before their tenth birthday. Nine patients were treated by bracing and it was ineffective in all (i.e. 0 % success with a brace), despite wearing it for an average of 11 h/day for a mean of 3.3 years. The most common curve pattern was a double major curve (right thoracic and left lumbar) and 12 patients were treated with surgery. The curve magnitude ranged from 60° to 80° at the time of surgery. Instrumented posterior spinal fusion (PSF) was performed using Luque wires in five and a Harrington rod in four patients. Posterior instrumentation with Luque wires and a Harrington rod without fusion was performed in the remaining three patients. Anchor dislodgement and rod breakages were a rule, rather than an exception, and revision surgery was needed in five patients. They reported a modest 20 % mean correction of scoliosis at the 5 year follow-up, with the mean longevity being 13 years (range: 7–25 years). The overall results of bracing for MFS are poorer than those for idiopathic scoliosis, and the results of one reported study were 17 % [35].

Conventional growing rods (CGR) had been the mainstay in the surgical management of EOS in MFS in the past. Dual rods, inserted subcutaneously, subfascially, or submuscularly were the standard of care until the end of the last decade. They could be inserted by making two tiny skin incisions, and then anchored to the proximal spine (or rib) anchors and spine (or pelvis) anchors distally, followed by rail-roading the growth rod linked with extensible domino or tandem connectors, which would be lengthened under general anaesthesia on a regular four to six monthly basis. Sponseller et al reported a series of ten patients treated with three single and seven dual growing rods and observed a mean curve correction of 51 % [36]. The mean age at surgery was 5.3 years and the mean duration of treatment with CGR was 5.25 years. Dual rods produced better correction than single rods, with reduced incidence of implant-related complications (anchor dislodgements and rod breakages). Definitive spinal fusion was performed on five patients after a mean of 5.5 years, following CGR insertion.

Magnet-driven growing rods (MdGR) are novel implants recently approved by USFDA and NICE for EOS and are the currently recommended standard of care for

all etiologies of EOS, with a remaining growth potential of at least 3 years [37]. They eliminate the need for invasive lengthenings under anaesthesia by office-based expansions and are reported to improve pulmonary function, especially in neuromuscular and syndromic scoliosis at 2 years [38]. There are at least five published studies reporting their early clinical results which are all very encouraging [39–43]. There are no published case reports to this day in the English language highlighting their use in MFS. The senior author (MHHN) has now inserted MdGR in a few MFS patients. Two such case examples of EOS secondary to MFS, treated by single and dual MdGR insertions, in two and a half and seven year old boys are illustrated in Figs. 12.3 and 12.4 respectively. A detailed description of our preferred surgical technique is as described below:

Surgical Technique

The patient was placed in prone position under general anaesthesia with endotracheal intubation on a Montreal mattress with adequate padding of all the pressure points. Special care was taken to avoid hyperextension of the upper extremities, which carried the risk of causing brachial plexopathy [44]. Pre-operative planning was undertaken to determine the anchor/instrumentation vertebrae guided by the curve characteristics. Our preference is to use a spine – spine anchor construct with all pedicle screw anchors for distal fixation and hybrid fixation for proximal anchors (pedicle screws and transverse process [TP] hooks). We prefer to have six points of proximal fixation and at least four distal fixation points in all cases. Abnormal lumbo-sacral transition or large dural ectasia with vertebral/sacral scalloping may warrant instrumentation to the pelvis and the use of iliac bolt fixation (our preferred method of pelvic fixation) or S2-Ala screws. Two separate skin incisions were made in the midline at the proximal thoracic spine (usually T2–T5 vertebra) and at the distal thoracolumbar/lumbar spine, exposing the predetermined fusion levels. Pedicle screws of appropriate length and diameter were inserted into the T3 and T4 vertebrae bilaterally by free-hand technique. Two down-going transverse process hooks were inserted into T2 and remained flush to the bone at all times in order to minimise the risk of apical pneumothorax. Two more pedicle screws were then inserted into the previously determined vertebrae as distal fixation anchors. A flexible rod template was used to measure the length of the rod needed and the MdGR was cut to the desired length. Care was taken to ensure that the actuator area containing the magnet remained straight at all times, which is crucial for the integrity of the magnetic coil system. Appropriate sagittal contouring dictated by the curve profile/patient characteristic was then given to the MdGR to facilitate the ease of insertion. The functioning of the magnetic coil was tested with the handheld device before its final insertion.

A 24G chest tube was then used to rail-road the rod submuscularly in a caudocranial fashion on the concave side and then it was attached to the fixation anchors, starting with the pedicle screws distally. The rod was attached to the hybrid construct cranially (hooks and pedicle screws). The posterior elements were then decorticated and mixed with bone marrow aspirate obtained at the time of the pedicle screw insertions. 10–20 mg of silicated calcium phosphate (SiCaP) granules were

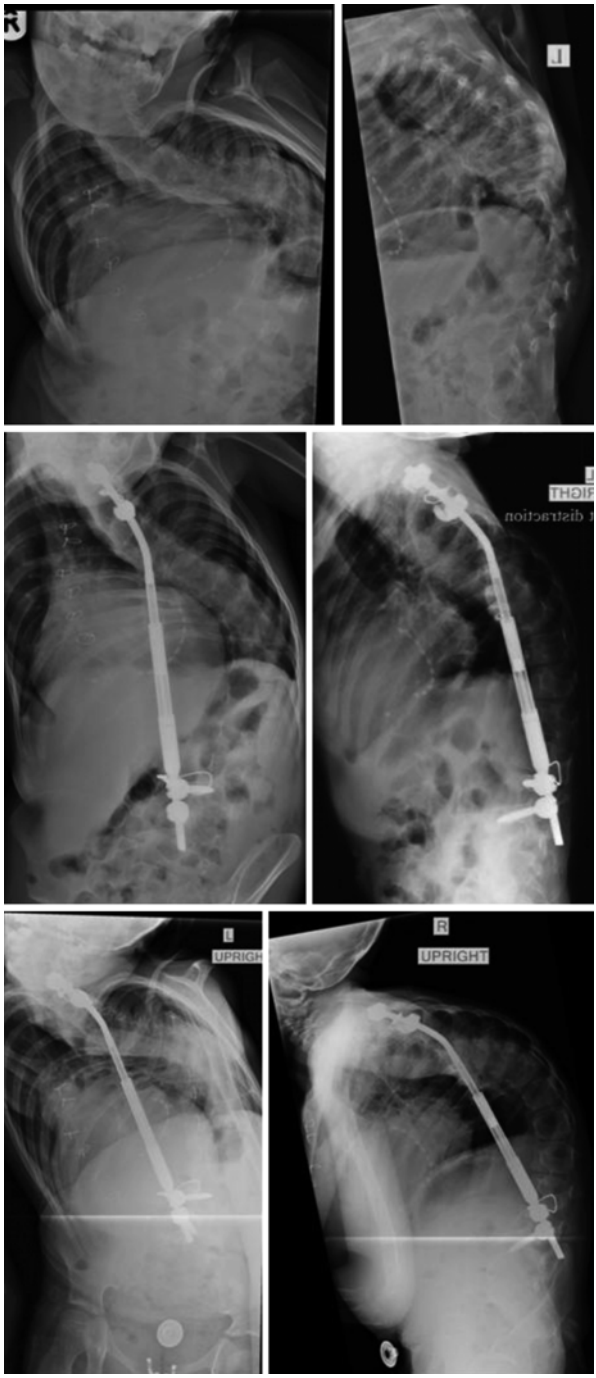

Fig. 12.3 A 2.5 year old Marfan syndrome boy with infantile kyphoscoliosis treated with a single submuscular insertion of a magnet-driven growing rod (MdGR). Preoperative, 1 year, and three and half years postoperative radiographs are shown

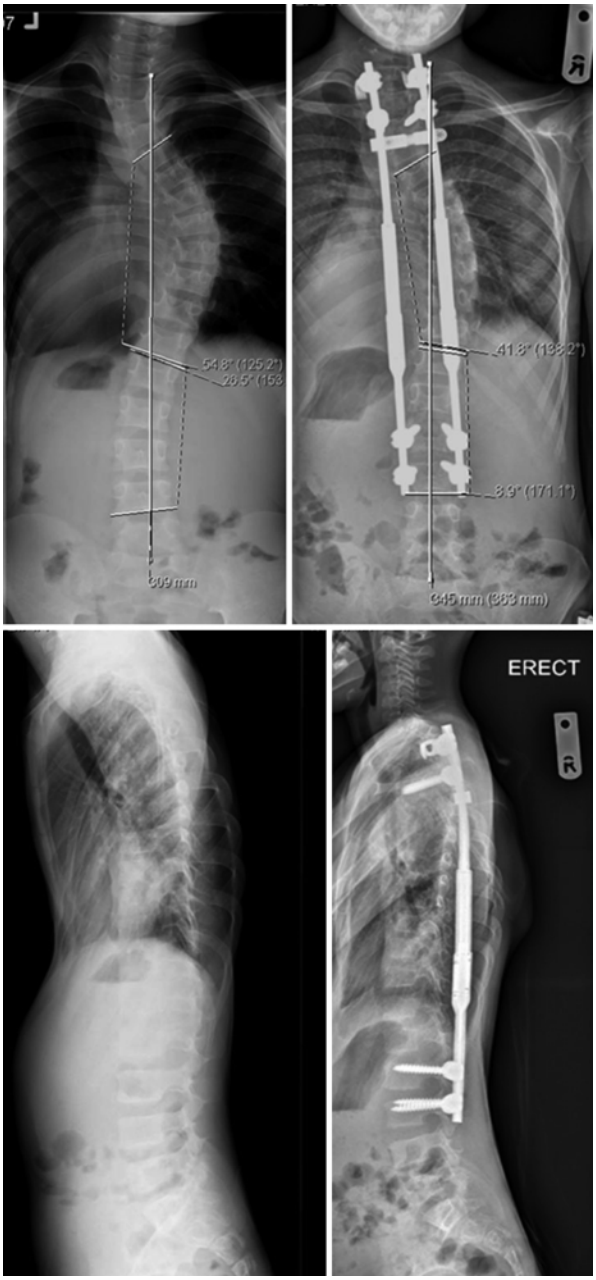

Fig. 12.4 A 7 year old Marfan syndrome boy with juvenile scoliosis and pectus excavatum treated with a novel magnet driven growing rod (MdGR) implant – dual rod insertion. Preoperative and postoperative PA and lateral radiographs are shown

mixed with native/host bone and then laid over both the proximal and distal fixation anchors. An index case, from a 7 year old child with juvenile MFS, illustrating our above technique with the use of a dual MdGR and having a T2–L3 fixation is shown in Fig. 12.4. Our preference is to use a dual rod construct whenever possible. We have used single rods (SR) in a few rigid multi-planar curves (especially those with severe kyphosis/kyphoscoliosis). SR are also particularly helpful for severe sagittal plane deformities, which provide flexibility with a creative design configuration and tension-free soft tissue/skin closure.

Post-operative Care and Rehabilitation

A chest radiograph is taken during recovery to ensure that the lung tissue is well expanded and rule out a spontaneous pneumothorax or secondary to TP hook insertion. The child should be allowed to sit-up, with head end elevated to 30°–40° with effect from day one and erect with effect from post-op day two. We let most of the children begin mobilisation from post-op on day two and they are discharged on day three or four. We do not routinely use orthosis following MdGR insertion, and we begin serial lengthening at 3 months post-op, and at two to three monthly intervals thereafter. Simple stretching exercises and school PT can be resumed at 3 months postoperatively. Contact sports and horse-riding are prohibited for at least 6 months. The initial 3 months of close observation with minimal physical activity ensures adequate arthrodesis at the anchor sites prior to commencing regular/serial distractions. All lengthenings are performed in office, wherein a handheld magnetic wand is used to locate the precise area of the magnetic coil. Low-dose chest x-rays or ultrasound (USG) are performed after each distraction to confirm that the spine has indeed lengthened and we document the distraction achieved in millimetres [45].

Traditional teaching in the past was to refrain from performing spinal surgery in patients aged <4 years, owing to the severe cardiac involvement, as large curve magnitude combined with poor cardiac reserve precluded one from undertaking surgical correction safely [34]. The rationale that such children would succumb spontaneously to cardiac failure was used to justify such a stand. Serial casting, though an option as a delaying tactic or time-buying strategy, is discouraged because of the restrictive effect it imposes on the lungs and its burden on cardiac physiology. However, with advances in infantile cardiac surgeries, this is being successfully challenged. One such case example of a 2.5 year old boy with neonatal MFS, presenting with severe kyphoscoliosis which was treated by a novel magnet-driven growing rod (MdGR) and operated on by the senior author with a follow-up of 3.5 years, is illustrated in Fig. 12.3. The top row depicts the preoperative radiographs (PA and Lateral) showing a left thoracic infantile scoliosis of ≥70°. A mean 22.3 mm length gain was achieved at one year post-op (middle row radiographs) following a single submuscular MdGR insertion. However, despite satisfactory curve containment in the coronal plane, there was a worsening of sagittal balance with thoracic hyperkyphosis at 3.5 years postoperatively (bottom row radiographs).

Such a phenomenon appears to be a rule than an exception, irrespective of the surgical option exercised. Early definitive spinal fusion is not recommended, as it causes a disproportionately short upper segment with a truncal height of <220 mm resulting in thoracic insufficiency syndrome (TIS) [46].

Adolescent and Adult Scoliosis in MFS

Surgical correction of scoliosis is eventually needed in at least 10–15 % of MFS patients [17, 18]. Definitive spinal fusion is usually performed when the patient has attained skeletal maturity/completed growth (i.e. Risser Gr. ≥IV). A preoperative MRI/CT scan is mandatory to evaluate for posterior element defect/dural ectasia to minimise the risk of durotomy during surgical exposure. Selective fusion of either the thoracic or thoraco-lumbar/lumbar curve is not recommended and long fusion tends to be the rule.

Unlike with idiopathic scoliosis, the surgical correction of MFS is associated with higher intraoperative blood loss, and the use of intraoperative anti-coagulants (i.e. é-amino caproic acid (EACA) or tranexemic acid) with an intraoperative cell-saver is recommended to minimise the blood loss. A higher incidence of inadvertent durotomy (8 %), pseudoarthrosis rate (21 %), deep infection (8 %), loss of correction achieved with time (30 %), laminar fractures (8 %) and implant failure (anchor dislodgement or rod breakage) is also reported [47, 48]. The ligamentous laxity and attenuated muscle tone pose unique sagittal plane challenges. MFS patients have a higher risk of developing proximal junctional kyphosis (PJK) or distal junctional kyphosis (DJK). Meticulous attention during surgical exposure with retention of the midline soft tissue structures (i.e. the supraspinous and interspinous ligaments) and inclusion of the first lordotic disc (on standing sagittal radiographs) in the instrumentation/construct minimises such events (i.e. PJK and DJK). Instrumentation to the pelvis may be inevitable in the presence of dural ectasia with vertebral scalloping.

Our preference is to correct the scoliosis using a low implant density index (IDI) construct (i.e. IDI of ≤1.5) with either all pedicle screws or a hybrid construct employing a combination of cantilever, translation, and derotation (CTD) techniques adhering to the Noordeen adolescent idiopathic scoliosis (AIS) curve classification algorithm to aid in the selection of fusion levels [49]. Our algorithm identifies three main curve patterns which are further subdivided into two sub-types (depending on the position of the shoulder on the convexity of the curve – i.e. up or down in relation to its counterpart on the concavity) yielding six different curve patterns as illustrated in Fig. 12.5. As a rule, we do not perform or recommend selective

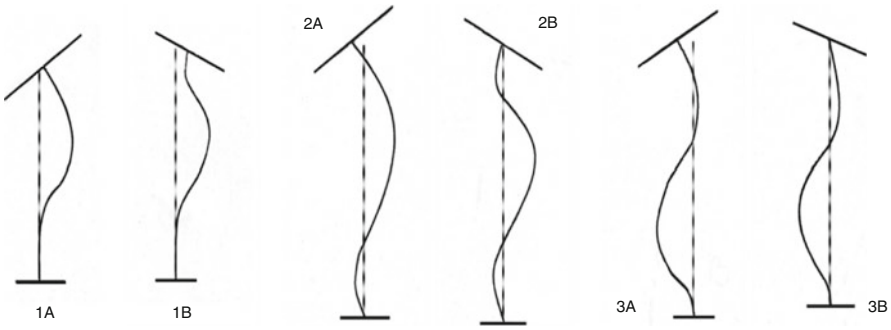

Fig. 12.5 The Noordeen AIS curve classification algorithm: six types of AIS curves. *1* structural thoracic curve. *2* structural thoracic & thoraco-lumbar/lumbar curve. *3* structural thoraco-lumbar/lumbar curve. Sub-types *A* convex shoulder is *up*. *B* convex shoulder is *down*

fusion of scoliosis in MFS. An index case example of such a correction in a 15 year old boy is illustrated in Fig. 12.6. We do not routinely use BMP or harvest an iliac crest bone graft (ICBG) to achieve arthrodesis. The gold standard ICBG is fraught with complications including, but not exclusively limited to, donor site morbidity, iliac wing fractures, prolonged hospital stay, iliac hematoma, etc. Our preference is to use silicated calcium phosphate (SiCaP) granules mixed with local autologous bone (spinous process and decorticated posterior elements) to achieve fusion. The use of a low IDI construct minimises implant costs associated with scoliosis correction without compromising clinical results or causing a loss of correction with time.

Practical Operative Tips to Improve Safety and Outcomes [48]

- Positioning the patient in the Trendelenburg position to minimise ballooning of the distal dura
- Avoiding the use of sublaminar wires to minimise the risk of inadvertent durotomy in the current era of pedicle screws which are '*gold standard*' anchors for surgical correction
- Aiming to achieve 50–60 % curve correction to avoid curve decompensation which could potentially result in excessive correction (i.e. >75 %)
- Avoid using laminar hooks as anchors (as there is a risk of laminar fractures and steel stenosis)
- Anaesthetic induction under the supervision of a cardiac anaesthetist with postoperative care in a cardiac ICU/cardiac floor, instead of a general orthopaedic or surgical floor.

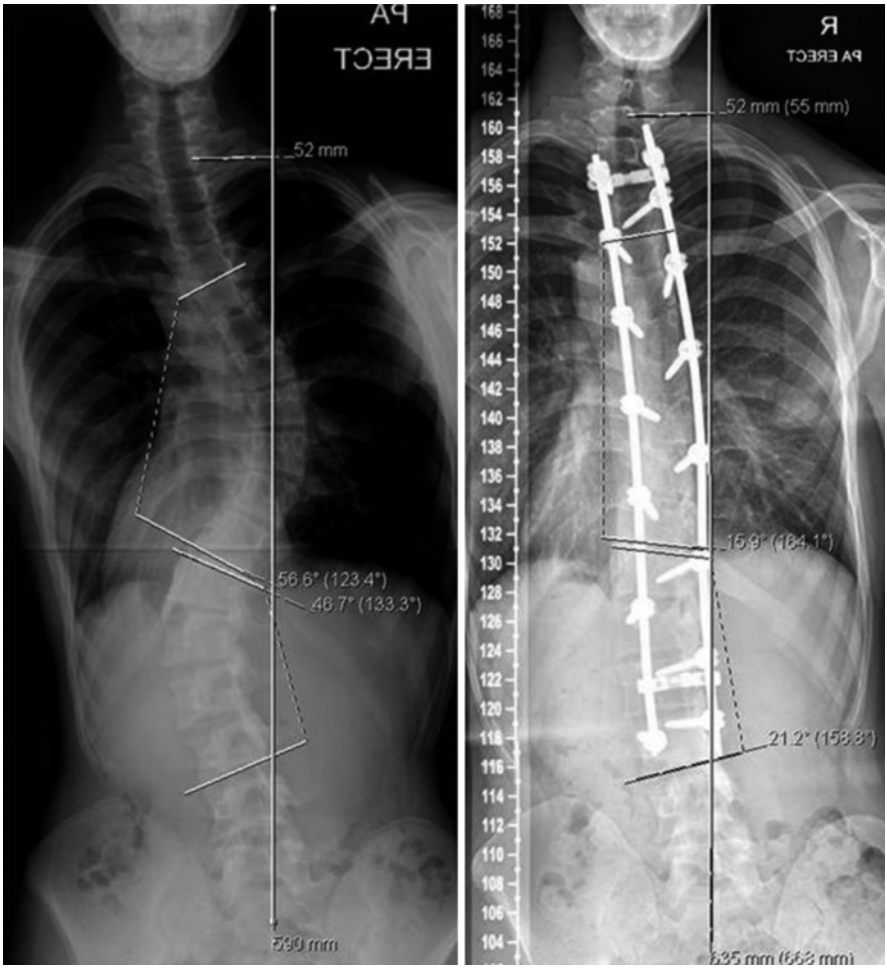

Fig. 12.6 A 15 year old Marfan syndrome boy with adolescent scoliosis treated with posterior instrumented spinal fusion using a low implant density index (IDI) construct. Preoperative and postoperative radiographs are shown

Conclusion

In summary, MFS is a systemic connective tissue disorder with scoliosis as one of its skeletal manifestations. Though the curve type and pattern mimics idiopathic scoliosis, distinct characteristics exists that differentiate MFS scoliosis from idiopathic scoliosis. Curves <20° largely remain unchanged and children should be observed until skeletal maturity for progression of the deformity. Bracing plays a small role, since scoliosis is usually resistant to bracing with poorer results, and it is indicated for curves with a Cobb angle of 21°–40° in the juvenile age group. Serial casts and braces may delay the need for growing rod

insertion/growth guided procedures in infantile scoliosis or neonatal MFS, which is often most severe and extremely difficult to treat. Curves >40° usually progress, which ultimately warrants surgical management. Understanding the vertebral morphological differences of the scoliotic spine in MFS is of paramount importance when planning and executing surgical correction.

Neonatal MFS produces some of the most severe multi-planar spinal deformities with significant cardio-pulmonary compromise. These patients usually live up to young adulthood and beyond with advances in cardiac care and pharmacotherapeutic treatment with β-blockers and Angiotensin converting enzyme (ACE) inhibitors [50]. Advances in growing rod technology with magnet-driven growing rods (MdGRs) are a boon to such vulnerable young children, since they eliminate the need for repetitive anesthesia and serve as an internal brace, guiding the curve correction with growth. Early definitive spinal fusion is not recommended, for it leaves an individual with a short trunk, manifesting with thoracic insufficiency syndrome (TIS) [46].

Juvenile scoliosis in MFS is best treated by bracing for moderate curves, and then growth guided procedures for those with severe/progressive curves (i.e. Growing rods: magnet-driven or conventional/Shilla technique/Luque-Trolley instrumentation, etc). MdGRs are increasingly becoming the standard of care for most aetiologies of early-onset scoliosis (EOS) and MFS is no exception. They have an added advantage of facilitating minimal absence from school, with normal psychological maturation, scholastic performance, with one-off surgery and serial office-based lengtheni.ng.

Patients with MFS needing scoliosis surgery have a higher risk of curve decompensation with excessive correction, incidental durotomy, and perioperative complications, compared to surgically treated idiopathic scoliosis patients [47, 48]. Dural ectasia (DE) may pose significant challenges and warrant instrumentation to the pelvis in select cases, owing to poor bone stock or vertebral scalloping which has a higher complication rate (i.e. pseudoarthrosis and implant failure).

Co-existent chest cage deformities may warrant surgery to increase the AP diameter of the chest and normalise the space available for the lungs (SAL) by using a Nuss bar for pectus excavatum [51]. The Nuss bar may cause a worsening of the kyphosis with paraparesis, warranting a high-risk vertebral column resection (VCR), and treating surgeons should be aware of this potential scenario [52]. The surgical correction of scoliosis in MFS should be undertaken at specialist centers with multi-modal intraoperative neuro-monitoring (IONM) in a safe manner. A preoperative work-up with CT/MRI/DEXA scans and medical optimisation and attention to detail improves the surgical outcome and final results.

Acknowledgements The authors would like to acknowledge Dr. JH Perra, MD, FACS – Attending spinal surgeon; Twin Cities Spine Center and Gillette Children's Specialty Healthcare – Minneapolis, MN, U.S.A for providing us with the pictures of the rapid prototyping (RP) model and 3D-CT images of a congenital spinal deformity (Fig. 12.1).

Conflict of Interest (CoI)

1. NS Harshavardhana: No relationships
2. Mohammed H. H. Noordeen:
   Ellipse Tech, Inc. – Consultant and stockholder
   K2M – Consultant
   Stryker Spine – Research and educational support (no period)

Authorship Contribution Statement The two authors (i.e. NSH and MHHN) jointly wrote and made substantial contributions in drafting the outline for the chapter. The clinical case example radiographs are from patients operated upon by MHHN. Both the authors read and approved the final draft of the submitted manuscript. We take full responsibility for the contents of this publication, attesting to both its accuracy and integrity, and we agree to be accountable for all aspects of the work.

References

1. Marfan AB. Un cas de déformation congénitale des quatre membres, plus prononcée aux extrémités caractérisée par l'allongement des os avec un certain degré d'amincissement. Bull Mem Soc Med Hop Paris. 1896;13:220–6.
2. Dietz HC, Pyeritz RE, Hall BD, et al. The Marfan syndrome locus: confirmation of assignment to chromosome 15 and identification of tightly linked markers at 15q15–q21.3. Genomics. 1991;9:355–61.
3. Dietz HC, Cutting GR, Pyeritz RE, et al. Marfan syndrome caused by a recurrent de novo missense mutation in the fibrillin gene. Nature. 1991;352:337–9.
4. Gray JR, Bridges AB, Faed MJ, et al. Ascertainment and severity of Marfan syndrome in a Scottish population. J Med Genet. 1994;31:51–4.
5. Frédéric MY, Monino C, Marschall C, et al. The FBN2 gene: new mutations, locus-specific database (Universal Mutation Database FBN2), and genotype-phenotype correlations. Hum Mutat. 2009;30:181–90.
6. Sakai H, Visser R, Ikegawa S, et al. Comprehensive genetic analysis of relevant four genes in 49 patients with Marfan syndrome or Marfan-related phenotypes. Am J Med Genet A. 2006;140:1719–25.
7. Silverman DI, Burton KJ, Gray J, et al. Life expectancy in the Marfan syndrome. Am J Cardiol. 1995;75:157–60.
8. Pyeritz RE, Francke U. The Second International Symposium on the Marfan syndrome. Am J Med Genet. 1993;47:127–35.
9. Dean JC. Marfan syndrome: clinical diagnosis and management. Eur J Hum Genet. 2007;15:724–33.
10. Keech MK, Wendt VE, Read RC, et al. Family studies of the Marfan syndrome. J Chronic Dis. 1966;19(1):57–83.
11. Fahey J. Muscular and skeletal change in arachnodactyly. Arch Surg. 1939;39:741–60.
12. Sinclair RJG, Kitchin AH, Turner RWD. The Marfan syndrome. Quart J Med. 1960;29:19–46.
13. Wilner HI, Finby N. Skeletal manifestation in the Marfan syndrome. JAMA. 1964;187:490–5.
14. Scheier H. Prognose und Behandlung der Skoliose. Stuttgart: Thieme publishers; 1967. pp. 15–21.
15. Ford J. Scoliosis in Marfan syndrome. Los Amigos Hospital (UCLA School of Medicine): Resident research reports; 1968.
16. Sliman NA. A propos de 16 cas de scoliosis. Marfan Tunisie Med. 1971;2:93–101.

17. Robins PR, Moe JH, Winter RB. Scoliosis in Marfan's syndrome: its characteristics and results of treatment in thirty-five patients. J Bone Joint Surg Am. 1975;57(3):358–68.
18. Sponseller PD, Hobbs W, Riley 3rd LH, Pyeritz RE. The thoracolumbar spine in Marfan syndrome. J Bone Joint Surg Am. 1995;77(6):867–76.
19. Demetracopoulos CA, Sponseller PD. Spinal deformities in Marfan syndrome. Orthop Clin North Am. 2007;38(4):563–72.
20. Sanghera B, Naique S, Papaharilaou Y, Amis A. Preliminary study of rapid prototype medical models. Rapid Prototyping J. 2001;7(5):275–84. What happened to the colon?.
21. Guarino J, Tennyson S, McCain G, et al. Rapid prototyping technology for surgeries of the pediatric spine and pelvis: benefits analysis. J Pediatr Orthop. 2007;27(8):955–60.
22. Grahame R, Pyeritz RE. The Marfan syndrome: joint and skin manifestations are prevalent and correlated. Br J Rheumatol. 1995;34:126–31.
23. Hobbs WR, Sponseller PD, Weiss AP, Pyeritz RE. The cervical spine in Marfan syndrome. Spine. 1997;22(9):983–9.
24. Oosterhof T, Groenink M, Hulsmans FJ, et al. Quantitative assessment of dural ectasia as a marker for Marfan syndrome. Radiology. 2001;220:514–8.
25. Ahn NU, Sponseller PD, Ahn UM, et al. Dural ectasia in the Marfan syndrome: MR and CT findings and criteria. Genet Med. 2000;2(3):173–9.
26. Pyeritz RE, Fishman EK, Bernhardt BA, Siegelman SS. Dural ectasia is a common feature of the Marfan syndrome. Am J Hum Genet. 1988;43(5):726.
27. Sponseller PD. Chapter 103 – Spinal deformities in Marfan syndrome. ridwell KH, De Wald R, editors. The textbook of spinal surgery. 3rd ed. Philadelphia: Lippincott, Williams & Wilkins; 2012.
28. Winter RB. Severe spondylolisthesis in Marfan's syndrome: report of two cases. J Pediatr Orthop. 1982;2(1):51–5.
29. Taylor LJ. Severe spondylolisthesis and scoliosis in association with Marfan's syndrome. Case report and review of the literature. Clin Orthop Relat Res. 1987;221:207–11.
30. Giampietro PF, Peterson M, Schneider R, et al. Assessment of bone mineral density in adults and children with Marfan syndrome. Osteoporos Int. 2003;14(7):559–63.
31. Sponseller PD, Jones KB, Ahn NU, et al. Protrusio acetabuli in Marfan syndrome: age-related prevalence and associated hip function. J Bone Joint Surg Am. 2006;88(3):486–95.
32. James JIP. The etiology of scoliosis. J Bone Joint Surg (Br). 1970;52:410–9.
33. Lenke LG, Dobbs MB. Management of juvenile idiopathic scoliosis. J Bone Joint Surg (Am). 2007;89 suppl 1:55–63.
34. Sponseller PD, Sethi N, Cameron DE, Pyeritz RE. Infantile scoliosis in Marfan syndrome. Spine. 1997;22(5):509–16.
35. Sponseller PD, Bhimani M, Solacoff D, Dormans JP. Results of brace treatment of scoliosis in Marfan syndrome. Spine. 2000;25(18):2350–4. No italics for title of journal?.
36. Sponseller PD, Thompson GH, Akbarnia BA, et al. Growing rods for infantile scoliosis in Marfan syndrome. Spine. 2009;34(16):1711–5.
37. The MAGEC system for spinal lengthening in children with scoliosis. NICE medical technology guidance (MTG18). https://www.nice.org.uk/guidance/mtg18. Accessed 8, 2015.
38. Yoon WW, Sedra F, Shah S, et al. Improvement of pulmonary function in children with early-onset scoliosis using magnetic growth rods. Spine. 2014;39(15):1196–202.
39. Cheung KM, Cheung JP, Samartzis D, et al. Magnetically controlled growing rods for severe spinal curvature in young children: a prospective case series. Lancet. 2012;379(9830):1967–74.
40. Akbarnia BA, Cheung K, Noordeen H, et al. Next generation of growth-sparing techniques: preliminary clinical results of a magnetically controlled growing rod in 14 patients with early-onset scoliosis. Spine. 2013;38(8):665–70.
41. Dannawi Z, Altaf F, Harshavardhana NS, et al. Early results of a remotely-operated magnetic growth rod in early-onset scoliosis. Bone Joint J. 2013;95-b(1):75–80.
42. Akbarnia BA, Pawelek JB, Cheung KMC, et al. Traditional growing rods versus magnetically controlled growing rods for the surgical treatment of early-onset scoliosis: a case-matched 2-year study. Spine Deform. 2014;2(6):493–7.

43. Hickey BA, Towriss C, Baxter G, et al. Early experience of MAGEC magnetic growing rods in the treatment of early onset scoliosis. Eur Spine J. 2014;23 Suppl 1:S61–5.
44. Schwartz DM, Drummond DS, Hahn M, et al. Prevention of positional brachial plexopathy during surgical correction of scoliosis. J Spinal Disord. 2000;13(2):178–82.
45. Stokes OM, O'Donovan EJ, Samartzis D, et al. Reducing radiation exposure in early-onset scoliosis surgery patients: novel use of ultrasonography to measure lengthening in magnetically-controlled growing rods. Spine J. 2014;14(10):2397–404.
46. Karol LA, Johnston C, Mladenov K, et al. Pulmonary function following early thoracic fusion in non-neuromuscular scoliosis. J Bone Joint Surg Am. 2008;90(6):1272–81.
47. Gjolaj JP, Sponseller PD, Shah SA, et al. Spinal deformity correction in Marfan syndrome versus adolescent idiopathic scoliosis: learning from the differences. Spine. 2012;37(18):1558–65.
48. Jones KB, Erkula G, Sponseller PD, Dormans JP. Spine deformity correction in Marfan syndrome. Spine. 2002;27(18):2003–12.
49. Harshavardhana NS, Noordeen MH. Surgical results with the use of Silicated Calcium Phosphate (SiCaP) as bone graft substitute in Posterior Spinal Fusion (PSF) for Adolescent Idiopathic Scoliosis (AIS). Scoliosis. 2015;10(27):1–12.
50. Shores J, Berger KR, Murphy EA, Pyeritz RE. Progression of aortic dilatation and the benefit of long-term beta-adrenergic blockade in Marfan's syndrome. N Engl J Med. 1994;330:1335–41.
51. Nuss D, Kelly RE, Croitoru DP, et al. A 10-year review of a minimally invasive technique for the correction of pectus excavatum. J Pediatr Surg. 1998;33(4):545–52.
52. Sugrue PA, O'Shaughnessy BA, Blanke KM, et al. Rapidly progressive Scheuermann's disease in an adolescent after pectus bar placement treated with posterior vertebral-column resection: case report and review of the literature. Spine. 2013;38(4):E259–62.