CHANGES IN ADOLESCENT INTERVERTEBRAL DISCS, END PLATES AND BONE MARROW OF LUMBAR SPINE IN IDIOPATHIC THORACIC SCOLIOSIS AN MRI BASED STUDY

BY: DR AHMAD FAUZEY KASSIM

DISSERTATION SUBMITTED IN PARTIAL FULFILLMENT FOR THE DEGREE OF MASTER OF MEDICINE (ORTHOPAEDICS)

UNIVERSITI SAINS MALAYSIA

MAY 2010

CHANGES IN ADOLESCENT INTERVERTEBRAL DISCS, END PLATES AND BONE MARROW OF LUMBAR SPINE IN IDIOPATHIC THORACIC SCOLIOSIS AN MRI BASED STUDY

Dr Ahmad Fauzey Kassim

M. Med(Ortho)

Department of Orthopaedic

School of Medical Sciences, Universiti Sains Malaysia

Health Campus, 16150 Kelantan , Malaysia

Introduction : Intervertebral disc degeneration is known to occur as early as the first decade in normal individuals. In adolescent idiopathic thoracic scoliosis, the spinal curvature is thought to impart mechanical stresses on the lumbar spine. This in theory would lead to early degenerative discs changes, Modic changes and Schmorl's nodes as part of the whole degenerative process. We have developed the study with the aim to identify and grade lumbar intervertebral discs, end plates, bone marrow changes and Schmorl's nodes in adolescent idiopathic thoracic scoliosis patients.

Objectives : The aims of this study were to identify and grade the discs degeneration, Modic changes (vertebral end plates signal), bone marrow changes and Schmorl nodes of the lumbar spine below the thoracic scoliosis curve in idiopathic adolescent thoracic scoliosis. We also aimed to determine the association between thoracic spine curvature and discs degeneration, Modic changes, bone marrow changes and Schmorl's nodes.

Patients and methods : The study was conducted as cross sectional study involving adolescent idiopathic scoliosis patients treated in Universiti Sains Malaysia Hospital, Kubang Kerian, Kelantan. The period of study was 6 months from November 2009 till April 2010.

Results: The majority of discs changes in our study fell into grade II of Pfirrmann classification ranging from 50% – 95 %. Grade III accounted for the second biggest group ranging from 5%-42.5% while grade IV made up the remaining group ranging from 2.5%-7.5%. Interestingly, none of the discs were graded as Pfirrmann 1 indicating all discs below the thoracic curve displays some degree of degenerative changes. There were also no Pfirrmann grade 5 discs. Most changes occurs at L2/3 and L3/4 lumbar discs levels and confined to grade 2 and 3 of Pfirrmann classification. In our study, the Modic changes is seen in 6 (15%) out of 40 patients. We also found that type 1 Modic changes (66.7%) is more common in adolescent idiopathic scoliosis. In our study, only 5% of the lumbar discs were found to have Schmorls nodes. We also found out that there were no association between thoracic curve and Pfirrman disc changes, Modic changes and Schmorl's nodes.

Conclusion: The intervertebral discs of lumbar region in adolescent idiopathic thoracic scoliosis patients did show evidence of degenerative changes. This is demonstrated by absence of grade Pfirrmann 1(normal) discs. Modic changes(15%) and Schmorl's nodes(5%) are not commonly found in the lumbar discs of idiopathic thoracic scoliosis. The severity of thoracic spinal curvature was not proven to affect grades(Pfirrmann) of degenerative disc changes, Modic changes and Schmorls nodes. (all p value >0.05

Dr Abdul Halim Yusof : Supervisor

Dr Rohsila Muhammad : Co researcher

Acknowledgement

I would like to thank everybody who have been of great help and support to me in the completion of this research and dissertation.

First and foremost, (الحمدلله) "All praise is due to Allah, The Almighty".

Special mention has to be given to my supervisor who have supported me with his encouragement and knowledge. To Dr Abdul Halim Yusof , I thank you.

A very special thank you to Dr Rohsila Muhammad(radiologist), my co researcher for her invaluable expertise in reading the MRI films.

Also to all my teachers, PM Dr Wan Faisham Nu'man Wan Ismail, PM Dr Mohd Imran Yusof, PM Dr Abdul Razak Sulaiman, and fellow lecturers who stimulated my interest in knowledge and self improvisation.

And Dr Sarimah, who made statistic easier to swallow.

Last but not least, my beloved family, my deepest gratitude and love.

Thank you all.

Table of content

Abstrak

Cakera tulang belakang mula mengalami proses ‘degenerasi’ seawal dekad yang pertama lagi. Bagi pesakit skoliosis remaja, tulang belakang bahagian toraks yang bengkok memberikan tekanan yang tinggi kepada cakera di bahagian ‘lumbar’. Secara teori, ini akan mengakibatkan perubahan lebih awal kepada proses ‘degenerasi’ cakera, perubahan Modic dan nodul Schmorl. Sebelum ujian imbasan gelombang magnet (MRI) dicipta, tiada kaedah dapat digunakan untuk mengkaji cakera tulang belakang, sum-sum tulang dan nodul Schmorl’s. Pemeriksaan ini kini dapat dijalankan dengan tepat dan terperinci dengan bantuan MRI.

Kajian secara merentas kumpulan ini bertujuan mengkaji cakera tulang belakang, perubahan ‘Modic’,‘Schmorl’s nodes’ dan keadaan sum-sum tulang belakang pada pesakit skoliosis toraks remaja. Imej MRI dari 40 orang pesakit merangkumi 200 cakera tulang belakang telah dipilih untuk kajian sepanjang tempoh 6 bulan. Purata umur pesakit ialah 15.5 ± 2.7 tahun (julat dari 10 hingga 20). Purata sudut Cobb’s ialah 47.63° ± 14.1° (julat dari 20° hingga 80°). Pesakit adalah mereka yang menerima rawatan di klinik tulang belakang, Jabatan Ortopedik, Hospital Universiti Sains Malaysia dan telah dirujuk untuk menjalani pemeriksaan MRI. Imej MRI telah diperolehi dari pengkalan data radiologi yang terdapat di universiti ini dan telah dianalisa oleh seorang pakar radiologi. Sudut Cobb’s pada bahagian toraks telah dikira menggunakan gambar radiologi tulang belakang pesakit. Maklumat mengenai jantina dan umur pesakit telah diperolehi dari rekod perubatan pesakit. Keputusan kajian menunjukkan semua cakera tulang belakang pada bahagian ‘lumbar’ mengalami proses degenerasi dan kebanyakannya di tahap gred 2 dan 3 pada sistem klasifikasi ‘Pfirrmann’. Tiada cakera yang digredkan sebagai normal

(Pfirrmann 1). Perubahan ‘Modic’(15%) dan nodul ‘Schmorl’s(5%) jarang dapat dilihat pada bahagian ‘lumbar’. Tahap bengkok tulang belakang juga tidak dapat dibuktikan mempengaruhi tahap ‘degenerasi’ cakera tulang belakang, perubahan ‘Modic’ dan nodul ‘Schmorl’s’.(nilai p >0.05)

Kesimpulan dapat dibuat bahawa semua cakera tulang belakang bahagian ‘lumbar’ pada pesakit skoliosis remaja bahagian toraks mengalami proses ‘degenerasi’. Tahap ‘degenerasi’ cakera tulang belakang juga tidak mempunyai kaitan yang jelas dengan tahap bengkok tulang belakang toraks.

Kata kunci: skoliosis remaja; cakera tulang belakang; perubahan ‘Modic’; ‘Schmorl’s nodes’; tulang belakang toraks bengkok

Abstract.

Intervertebral disc degeneration is known to occur as early as the first decade in normal individuals. In adolescent idiopathic thoracic scoliosis, the spinal curvature is thought to impart mechanical stresses on the lumbar spine. This in theory would lead to early degenerative discs changes, Modic changes and Schmorl's nodes as part of the whole degenerative process. Before the advent of magnetic resonance imaging (MRI), proper assessment of the discs, end plates, vertebral bone marrow changes and Schmorl's nodes were not possible. With the help of MRI, a more detailed and accurate assessment of the intervertebral disc and vertebral bone marrow is now possible.

This was a cross sectional study with the aim to identify and grade lumbar intervertebral discs, end plates, bone marrow changes and Schmorl's nodes in adolescent idiopathic thoracic scoliosis patients. Lumbar MRI films from 40 patients totaling 200 discs were recruited into this study during 6 month period. The patients' ages were 15.5 ± 2.7 years old (range 10 to 20). The Cobb's angles average were 47.63° ± 14.1° (range 20° to 80°). The patients were those attending Spine clinic, Hospital Universiti Sains Malaysia and diagnosed with idiopathic thoracic scoliosis. MRI were ordered for them mainly due to complaints of back pain, neurological deficit and others. MRI films were obtained from the online database system and analyzed by a radiologist, looking for the changes mentioned before. Thoracic scoliosis Cobb's angles were measured from patient's AP(anteroposterior) radiological film of the spine. Demographic data regarding sex and age were obtained from the patients' medical records. Our results showed that in adolescent idiopathic thoracic scoliosis patients, all lumbar discs were affected by degenerative changes mainly grade 2 and 3 in Pfirrmann classification system. No disc

was graded as normal (Pfirrmann 1). Modic changes(15%) and Schmorl's nodes(5%) are not commonly found in the lumbar discs of idiopathic thoracic scoliosis. The severity of thoracic spinal curvature was not proven to affect grades (Pfirrmann) of degenerative disc changes, Modic changes and Schmorls nodes. (all p value >0.05)

We concluded that lumbar discs in adolescent idiopathic scoliosis with a single thoracic curve are all affected by degenerative changes. The thoracic curvature was not proven to have a direct effect on the severity of disc changes, Modic changes and Schmorl's nodes.

Keyword: idiopathic scoliosis; intervertebral discs; Modic changes; Schmorl's nodes; thoracic curvature

CHAPTER 1.

1.0 Introduction

Adolescent idiopathic scoliosis (AIS) is a structural, lateral, rotated curvature of the spine with changes in sagittal profile that arises in otherwise healthy children at or around puberty. The diagnosis is one of exclusion, and is made only when other causes of scoliosis, such as vertebral malformation, neuromuscular disorder, and syndromic disorders, have been ruled out. Patients are generally screened with Adams' forward bending test to rule out functional scoliosis. In the frontal plane the normal load-bearing spine is straight. Scoliosis is defined as a deviation from the midline in a frontal plane. A small deviation $< 10°$ is sometimes called spinal asymmetry, whereas "true" scoliosis has a deviation of $\geq 10°$. This deviation is accompanied by a rotation that is maximum at the apex of the curve.

Scoliosis curves can range from mild to severe type of deformity. The effect of this deformity on the individual is variable, causing cosmetic abnormalities and hence psychological effects in many patients and, at its most severe, life-threatening respiratory compromise due to thoracic cage deformity. Loads acting on scoliotic spines are thought to be asymmetric and involved in progression of the scoliotic deformity. Abnormal loading patterns theoretically can lead to changes in bone and disc cell activity and hence to vertebral body and disc wedging. Meir et al proceeded to obtain quantitative measurements of the intradiscal stress environment in scoliotic intervertebral discs and determine if loads acting across the scoliotic spine are asymmetric (Meir & Fairbank et al 2007). They performed in vivo measurements of stresses across the intervertebral disc in patients with scoliosis, both parallel (termed horizontal) and perpendicular (termed

vertical) to the end plate, using a side mounted pressure transducer (stress profilometry). Results were compared with similar stress profiles measured during surgery across 10 discs of 4 spines with no lateral curvature and with data from the literature. They have shown that profiles across scoliotic discs were very different from those of normal, young, healthy discs of equivalent age previously presented in the literature. Hydrostatic pressure regions were only seen in 14/25 discs, extended only over a short distance. Non-scoliotic discs of equivalent age would be expected to show large centrally placed hydrostatic nuclear regions in all discs. Mean pressures were significantly greater (0.25 MPa) than those measured in other anaesthetised patients (<0.07 MPa). A stress peak was seen in the concave annulus in 13/25 discs. Stresses in the concave annulus were greater than in the convex annulus indicating asymmetric loading in these anaesthetised, recumbent patients. From these findings, they concluded that intradiscal pressures and stresses in scoliotic discs are abnormal, asymmetrical and high in magnitude even in the absence of significant applied muscle loading.

In another study by Buttermann & Beaubien et al, they performed a biomechanical human cadaveric study comparing straight and simulated scoliotic spines with healthy and degenerated L4/L5 lumbar discs (Buttermann & Beaubien et al 2008). Their objective was to determine the conditions of discs under various spinal alignments by measuring the coronal intradiscal pressure profiles. Intradiscal pressure profiles for the L4/5 disc and resultant moments were obtained under axial follower loads up to 1500 N. They found that scoliosis significantly increased coronal moments ($P < 0.003$). Disc pressures increased linearly with greater applied loads for all specimens. Healthy L4/5 discs exhibited uniform pressure profiles with normal spinal alignment and minimal

effect with simulated scoliosis. For degenerated discs, there was a relative pressure profile depression in the nucleus relative to the anulus region. Furthermore, with spinal malalignment due to scoliotic curvature, there was disc pressure profile asymmetry. The ratio of maximum intradiscal pressure at the concavity relative to the convexity was 1.1 (range, 1.0-1.2) for healthy discs and 3.6 (range, 2.2-4.4) for degenerated discs in the scoliotic specimens ($P = 0.008$). The conclusion made was that disc pressure profilometry below long spinal constructs found asymmetric loading with the greatest loads at the concave inner anulus, especially in the presence of disc degeneration and scoliosis. For the degenerated cases, there was substantial disc pressure profile asymmetry despite only mildly severe scoliotic curvatures. These results suggest a compounding effect of asymmetric loading and progression of disc degeneration.

The possible mechanical and biological consequences of high or asymmetrical pressures and stresses in the spine can be divided into affects on the vertebral body and end plate or on the disc itself. The growth plate of the vertebral body has been shown to be sensitive to mechanical influences, with sustained loading causing reduction in the size of hypertrophic chondrocytes and reduction in the number of proliferating cells (Stokes & Mente et al 2002). The composition of the disc matrix and hence its material properties are also directly affected by hydrostatic pressure changes and changes in osmotic pressure and fluid movement acting directly on the intervertebral disc cells.(Handa & Ishihara et al 1997). Finally, in addition to these biological effects, abnormal loading can cause shape changes due to creep of the viscoelastic disc with fluid flow occurring both within and from the disc to surrounding structures. This fluid movement can cause further secondary effects such as nucleus depressurization and

compressive loading of the annulus with subsequent deleterious effects to these structures.

Classically, majority of AIS patients do not present with back pain but increasing number of studies have shown this to be not necessarily true. A study by Ramirez et al. showed a 23% prevalence of pain in patients with a presumed diagnosis of idiopathic scoliosis (Ramirez et al., 1997**).** He performed a retrospective study of 2442 patients who had idiopathic scoliosis to determine the prevalence of back pain and its association with an underlying pathological condition**.** He found a significant association between back pain and an age of more than fifteen years**,** skeletal maturity (a Risser sign of 2 or more), post-menarchal status, and a history of injury. There was no association with gender, family history of scoliosis**,** limb-length discrepancy, magnitude or type of curve, or spinal alignment.

However, in a study by Buttermann, G.R. et al, they found that degenerated discs themselves did not contribute to presence of low back pain. They actually associated presence of end plates changes and Schmorl's nodes with low back pain in scoliosis. (Buttermann and Mullin et al., 2008)

Previously, magnetic resonance imaging (MRI) was used to assess soft tissues of the spine and previous MRI studies of scoliosis patients have assessed abnormalities of the spinal canal or cord (Davids & Chamberlin et al 2004). The MRI is also useful for assessment of degenerative changes in the disc, such as loss of hydration leading to degeneration, Schmorl's nodes, and inflammatory endplate changes. However, studies using MRI in scoliosis patients are very difficult to find in the literature. This study has been put forward in an attempt to shed some light in this aspect.

CHAPTER 2

2. Literature review

2.1 Intervertebral disc anatomy and degeneration

2.1.1 Anatomy

The intervertebral discs are cartilaginous, articulating structures between the vertebral bodies that allow movement (flexion, extension, and rotation) in the otherwise rigid anterior portion of the vertebral column. The discs form a very complex system, with an outer anulus fibrosus surrounding a central nucleus pulposus. Collagen fibers continue from the anulus into the adjacent tissues, tying this fibrocartilaginous structure to the vertebral bodies at its rim, to the longitudinal ligaments anteriorly and posteriorly, and to the hyaline cartilage end plates superiorly and inferiorly. The cartilage end plates in turn lock into the osseous vertebral end plates via the calcified cartilage.

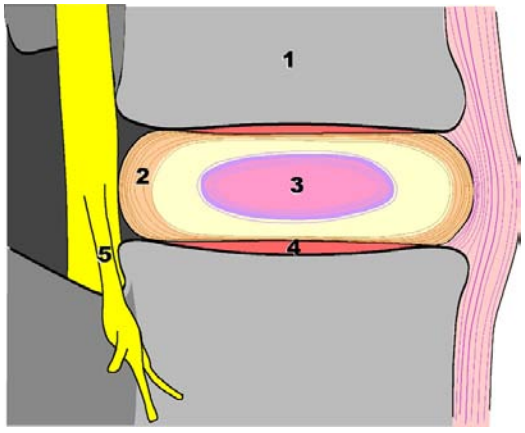

Figure 1. Diagram of sagittal section of vertebral body and disc showing relationship of endplate and longitudinal ligament to the disc and the vertebrae. 1, vertebral body; 2, annulus fibrosus; 3, nucleus pulposus; 4, endplate; 5, spinal nerve root.
(Adapted from Hariharan Shankar et al 2009, 'Anatomy and pathophysiology of intervertebral disc disease'. Techniques in Regional Anesthesia and Pain Management, Volume 13, Issue 2, April 2009, Pages 67-75)

2.1.2 Changes with age

A previous study has reported as early as two years of age, mild microscopic degenerative changes are seen, including decay and/or proliferation of nucleus pulposus cells, alterations in cell density and matrix degeneration in the cartilage end plate. This is thought to coincide with regression of blood vessels in the anulus, cartilage, and osseous end plates (Boos et al., 2002). It has also been observed in this study that the disc undergoes degenerative changes earlier in life than other tissues. It is likely that the rapid reduction in nutrient supply contributes to this early degeneration.

2.1.3 Pathophysiology of disc degeneration

The degenerative process begins in the nucleus pulposus (NP) with cell loss and matrix alteration. Progression of disease causes the outer annulus fibrosus (AF) to lose its normal lamellar arrangement and compromises the mechanical strength of the disc. As the disc fails, tissue fissures and clefts progress from the inner AF outward and contribute to the loss of mechanical integrity. These changes increase the mechanical forces transferred to the surrounding vertebral end plates and cause microfractures and marginal osteophyte formation (Berlemann et al., 1998). Cytokines produced within the disc stimulate ingrowth of nerve and vascular elements that may play a role in the etiology of spinal pain. Although this sequence happens during life in essentially all humans, there are significant variations in the degree of symptoms noted by different people (Freemont et al., 2002). There is also little known about correlation between the degree of degenerative changes noted on imaging studies and the presence of symptoms of spinal pain.

2.2 Pathogenesis of adolescent idiopathic scoliosis

Despite extensive studies, the understanding of etiology in AIS remains a mystery. The identification of etiological factors will depend on continued research in possible areas listed below. A better understanding of this disorder will enable the clinician to better predict prognosis and to aid in the development of more effective treatment modalities.

The areas of studies on suggested etiological factors :

a) **Genetic factors**

The role of hereditary or genetic factors in the development of idiopathic scoliosis has been widely accepted as one of the possibilities. Clinical observations as well as population studies have documented scoliosis within families, with the prevalence higher among relatives than within the general population (Filho and Thompson, 1971). Studies on scoliosis twins have further supported the genetic basis of AIS. A twin study compared the clinical similarity of monozygotic (MZ), or identical, twins who share 100% of their genes, to that of dizygotic (DZ,) or fraternal, twins who share only 50% of their genes. A concordance for idiopathic scoliosis was 92.3% in monozygotic twins and 62.5% in dizygotic twins. 70% of the monozygotic twins also had similar back shape (Inoue et al., 1998). A meta-analysis by Kesling et al on these clinical twin studies revealed 73% MZ concordances compared to 36% DZ concordances. Interestingly, when curve measurements were compared between monozygous twins, the correlation

coefficient was significantly greater than the same correlation measurement between dizygous twins ($P < 0.0002$). (Kesling and Reinker et al 1997)

A more recent report utilizing the Danish Twin Registry found 25% concordance in monozygotic twins (6 of 44 concordant) compared to 0% concordance (0 of 91) in dizygotic twins, with an overall prevalence of approximately 1%. The lower concordances in both groups as compared with prior results may be explained by differences in methodology, i.e., ascertainment in clinics vs. registry and screening by examination vs. questionnaire. Nevertheless, the overall trend obtained for all studies suggests strong genetic effects in AIS. A second important feature of AIS revealed by these studies was that monozygotic twins shared disease less than 100% of the time, reflecting the complexity of disease and suggesting the involvement of unknown factors in disease susceptibility. (Andersen and Thomsen et al 2007)

Despite documentation of the familial nature of this condition, the mode of inheritance has been debated. Studies based on a wide variety of populations have suggested an autosomal dominant, X-linked, or multifactorial inheritance pattern although so far, a conclusion has not been made.

b) **Role of melatonin**

In 1983, Dubousset et al. found that scoliosis routinely developed in pinealectomized chickens and attributed this effect to decreased melatonin production (Dubousset et. al., 1983). Dubousset and Machida went on to measure the levels of melatonin in thirty adolescents with idiopathic scoliosis and in fifteen age-matched

controls. The patients had severe scoliosis ranging from 57 to 75 degrees. The curves were divided into those that had progressed more than 10 degrees in the preceding year and those that had not. Patients with progressive scoliosis had a 35 percent decrease in melatonin levels throughout the night compared with those with stable scoliosis or the control subjects. (Machida and Dubousset et al 1996)

The diurnal variation in melatonin levels seems to be important in determining development of idiopathic scoliosis. However, scoliosis is not observed when this rhythm is obliterated in several diseases. Moreover, patients with idiopathic scoliosis do not normally present with sleep difficulties or immune function, which might be expected with a substantial decrease in melatonin. On this basis, it is more likely that melatonin plays a secondary role in the development of idiopathic scoliosis.

c) **Role of connective tissue**

Collagen and elastic fibers are principal elements in the supporting structures of the spinal column. As scoliosis is characteristic of many connective-tissue disorders, such as Marfan syndrome, the hypothesis that the connective tissue defect is the causative factor of idiopathic scoliosis is quite an acceptable opinion.

The morphology and composition of the intervertebral disc and cartilage end-plate were studied in patients with idiopathic or congenital scoliosis by Roberts S et al. He compared the findings to those obtained from autopsy as controls. The proteoglycan and water contents were reduced in both structures in specimens from scoliotic patients, particularly toward the concavity of the curve. The distribution of some collagen types also differed in tissue from scoliotic patients and autopsy tissue. Calcification of the

cartilage end-plate, and sometimes of the adjacent disc, occurred in all but three scoliotic patients, whereas there was minimal calcification in the autopsy specimens. They concluded that these changes are probably a secondary response to altered loading in the scoliotic patients. (Roberts et al., 1990)

The second major component of the extracellular matrix, elastic fiber has also been studied in individuals with idiopathic scoliosis. Elastic fibers are made up of two components: elastin core and microfibrils mainly consisting of fibrillin. A study was performed on the elastic fiber system of the ligamentum flavum in twenty-three patients who had scoliosis and in five age-matched individuals who did not. Fresh-frozen histological specimens of ligamentum flavum removed at the time of an operation were examined by Verhoeff staining for elastic fibers and by immunohistochemical staining with use of a monoclonal antibody to fibrillin (Hadley-Miller et al., 1994). They found elastic fiber abnormalities in the spinal ligaments in majority of patients with idiopathic scoliosis compared with normal individuals.

There is still divided opinion regarding the changes observed within the connective tissues of individuals with idiopathic scoliosis. The possibility of them to be the consequence of scoliosis rather than the causative factor is still being debated. However, most researchers concede that abnormalities reported in majority of individuals affected with idiopathic scoliosis are probably secondary to the structural forces of the scoliotic deformity itself. (Harrington, 1977)

d) **Skeletal muscle abnormalities**

Paraspinous muscles abnormality have been thought to be the cause of idiopathic scoliosis for many years. Two types of muscle fibers in paravertebral muscles of patients with adolescent idiopathic scoliosis have been described namely type-I (slow-twitch) and type-II (fast-twitch) fibers. It was found out that the number of type-II fibers was decreased in scoliotic patients, suggesting a myopathic process. A normal distribution of type-I and type-II fibers on the convexity of the curve but a lower frequency of type-I fibers on the concavity was found. (Bylund et al., 1987).

Other studies have reported findings of marked decrease in muscle spindles in the paraspinous muscles, increased calcium content due to generalized membrane defect and higher muscle protein synthesis on the convexity than on the concavity in patients(Slager and Hsu, 1986, Yarom et al., 1978). However, no definite conclusions can be reached with regard to involvement of skeletal muscle abnormalities as one of the etiology.

e) **Thrombocyte abnormalities (role of calmodulin)**

Calmodulin, a calcium-binding receptor protein, is a critical mediator of cellular calcium function and regulates many important enzymatic systems. Calmodulin regulates the contractile properties of muscles and platelets by interacting with actin and myosin and regulating calcium movement from the sarcoplasmic reticulum. Increased calmodulin levels in platelets have been shown to influence the progression in adolescent idiopathic scoliosis (Kindsfater et al., 1994). He studied on seventeen patients who had idiopathic scoliosis of varying severity and patterns and a control group consisting of ten age and sex-matched subjects. Level of platelet calmodulin in the patients who had a progressive

curve (more than 10 degrees of progression in the previous twelve months) (3.83 nanograms per microgram of protein) was significantly higher than the level in the patients who had a stable curve (less than 5 degrees of progression in the previous twelve months) (0.60 nanogram per microgram of protein) ($p < 0.01$). However, the levels in the stable group and the control group (0.69 nanogram per microgram of protein) were similar. He concluded that level of platelet calmodulin appeared to be an independent and possibly more acute predictor of progression of the curve.

f) **Neurological mechanisms**

Over the last twenty years, advanced neurological investigations have been used to compare idiopathic scoliosis patients with controls and to compare patients who have curves progression with those who have do not. However, the results have been inconsistent (Yekutiel et al., 1981). No proven neurological tests either for diagnosing idiopathic scoliosis or for predicting its progression have so far been established.

The advent of magnetic resonance imaging has led to renewed interest in abnormal neuroanatomy linked to scoliosis. MRI was performed in 31 scoliosis patients with onset between the ages of four and 12 years. In eight patients (26%) there was a significant neuroanatomical abnormality; there were six cases of Chiari-1 malformation associated with a syrinx, one isolated Chiari-1 malformation and one astrocytoma of the cervical spine. Four of these patients had left-sided curves. There were no clinical features which could reliably identify those patients with abnormalities on MRI. The unilateral absence of abdominal reflexes was found to be non-specific (1 of 8 of patients with neuroanatomical abnormalities (12.5%) versus 2 of 23 with normal scans (8.7%). It

is not yet known whether this is secondary to the syrinx formation as the first sign of syringomyelia or whether this asymmetry might reflect a more proximal hindbrain or midbrain lesion. Alternatively, the Chiari malformation and the syrinx could be the result of traction on the medulla distally through the foramen magnum.

2.3 Pfirrmann classification

Magnetic resonance imaging (MRI) is one of the most important method for the clinical assessment of intervertebral disc pathology. The signal characteristics of the disc in T2-weighted MRIs have been shown to reflect changes caused by aging or degeneration. (Pearce et al., 1991). The signal intensity of the disc in relation to chemical composition and histologic changes has also been studied. The brightness of the nucleus has been shown to correlate directly with the proteoglycan concentration, but not with the water or collagen content. (Tertti et al., 1991).

Few attempts have been made to classify the level of degenerative changes in the intervertebral discs. Most previous classification systems and reliability studies of lumbar disc abnormalities on MRI have focused on the posterior aspect of the disc, distinguishing among bulging, protrusion, and extrusion. Studies focusing on the MRI characteristics of the disc structure are rare. The ideal classification system for disc degeneration should be quantitative, permits region-specific evaluation within the disc sub-structures, avoids observer bias, can detect early subtle changes, and correlates with clinical symptoms.

Among the classification systems suggested is the classification developed by Pfirrmann which is based on the preliminary work by Pearce.. A grade between I and V is assigned based on signal intensity and structural morphology of the disc. (Pfirrmann et al., 2001). The classification is as illustrated in Table 1. In this study, three observers with different levels of experience analyzed spinal MRIs (*i.e.*, an orthopedic surgeon, a fellowship-trained musculoskeletal radiologist, and a musculoskeletal senior staff radiologist) and graded each of the 300 lumbar intervertebral discs on the T2-weighted sagittal images.

The appearance of MRI images for each grade is illustrated in Figure 2. Intraobserver agreement was excellent for all three readers, with kappa values ranging from 0.84 to 0.90 while interobserver agreement ranged from substantial to excellent, with kappa values ranging from 0.69 to 0.81. This is in accordance with Landis and Koch who rated the agreement as follows: kappa 0 to 0.2 indicated slight agreement, 0.21 to 0.4 fair agreement, 0.41 to 0.60 moderate agreement, 0.61 to 0.8 substantial agreement, and 0.81 upward excellent agreement. (Landis and Koch, 1977)

Pfirrmann also developed an algorithm to facilitate the process of grading the discs. This algorithm is shown in Figure 3. The authors also suggested adding the Modic classification (Types 1–3) to their grading system for further specification of a degenerated intervertebral disc in the case of concomitant end plate change. (Pfirrman et al., 2001). In order to achieve an objective assessment of the intervertebral discs in adolescent scoliosis patients, we have chosen this classification to help identify the degree of degeneration in the lumbar spine.

Table 1. Pfirrman classification of the intervertebral discs (Adapted from Pfirrmann, C. W. A., Metzdorf, A., Zanetti, M., Hodler, J., & Boos, N., (2001). Magnetic Resonance Classification of Lumbar Intervertebral Disc Degeneration. *Spine*, **26**(17)**,** 1873–1878)

Grade	**Structure of disc**	**Distinction of nucleus and anulus**	**Signal intensity**	**Height of disc**
I	Homogenous, bright white	Clear	Hyperintense, isointense to cerebrospinal fluid	Normal
II	Inhomogenous with or without horizontal bands	Clear	Hyperintense, isointense to cerebrospinal fluid	Normal
III	Inhomogenous, gray	Unclear	Intermediate	Normal to slightly decreased
IV	Inhomogenous, gray to black	Lost	Intermediate to hypointense	Normal to moderately decreased
V	Inhomogenous, black	Lost	Hypointense	Collapsed disc space

Explanation for the grading system of lumbar disc degeneration.

Grade I: The structure of the disc is homogeneous, with a bright hyperintense white signal intensity and a normal disc height.
Grade II: The structure of the disc is inhomogeneous, with a hyperintense white signal. The distinction between nucleus and anulus is clear, and the disc height is normal, with or without horizontal gray bands.
Grade III: The structure of the disc is inhomogeneous, with an intermediate gray signal intensity. The distinction between nucleus and anulus is unclear, and the disc height is normal or slightly decreased.
Grade IV: The structure of the disc is inhomogeneous, with an hypointense dark gray signal intensity. The distinction between nucleus and anulus is lost, and the disc height is normal or moderately decreased.
Grade V: The structure of the disc is inhomogeneous, with a hypointense black signal intensity. The distinction between nucleus and anulus is lost, and the disc space is collapsed.
Grading is performed on T2-weighted midsagittal (repetition time 5000 msec/echo time 130 msec) fast spin-echo images.

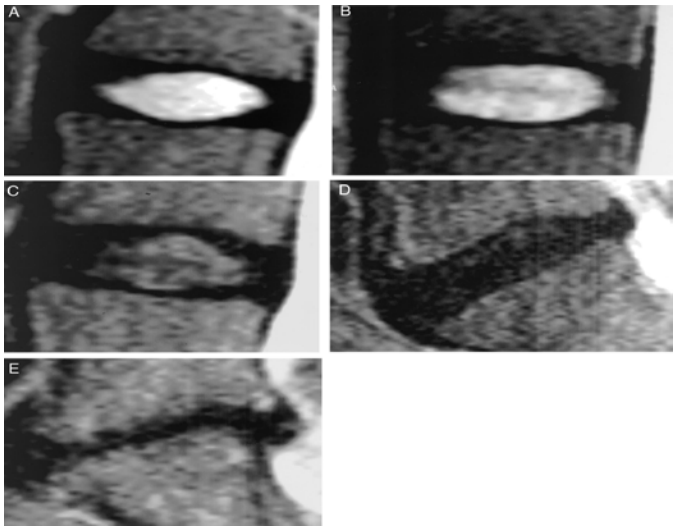

Figure 2. The changes seen on MRI films corresponding to Pfirrman grading.

(Adapted from Pfirrmann, C. W. A., Metzdorf, A., Zanetti, M., Hodler, J., & Boos, N., (2001). Magnetic Resonance Classification of Lumbar Intervertebral Disc Degeneration. *Spine*, **26**(17)**,** 1873–1878)

A – Grade I ,
B – Grade II
C – Grade III
D – Grade IV
E – Type V

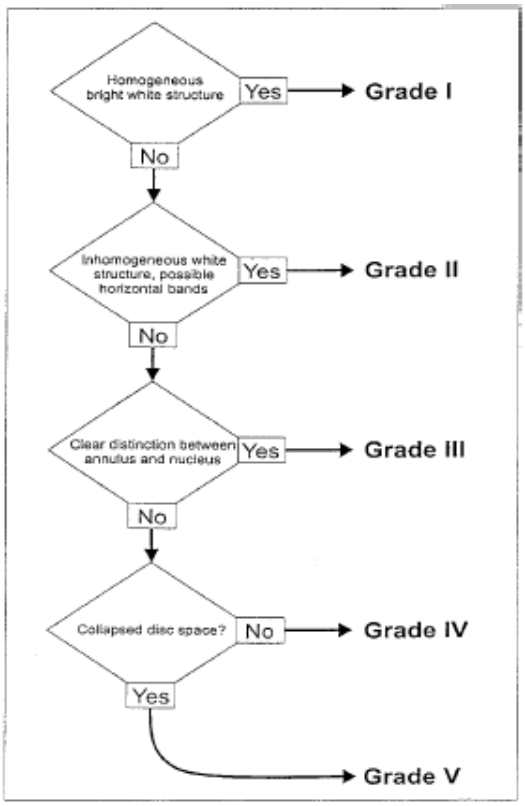

Figure 3. Algorithm suggested by Pfirrman to facilitate the grading of discs. (Adapted from Pfirrmann, C. W. A., Metzdorf, A., Zanetti, M., Hodler, J., & Boos, N., (2001). Magnetic Resonance Classification of Lumbar Intervertebral Disc Degeneration. *Spine,* **26**(17)**,** 1873–1878)