INCIDENCE OF ADJACENT SEGMENT DEGENERATION FOLLOWING SINGLE LEVEL DISCECTOMY AND SINGLE LEVEL INSTRUMENTED FUSION – A COMPARATIVE STUDY

A DISSERTATION SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENT OF THE TAMILNADU DR. M. G. R. MEDICAL UNIVERSITY, TAMIL NADU, CHENNAI FOR THE AWARD OF M.S. ORTHOPAEDICS DEGREE TO BE HELD IN APRIL 2015.

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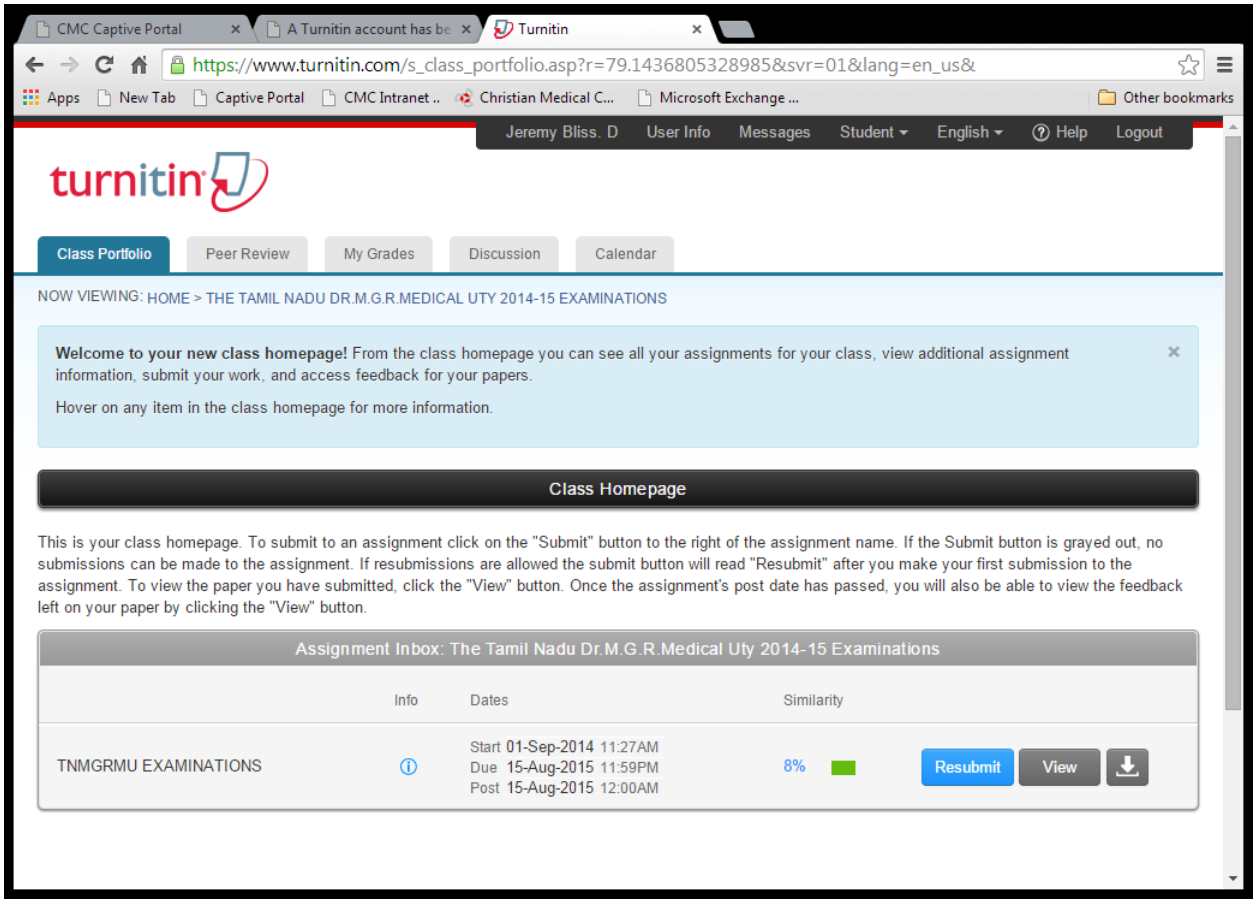
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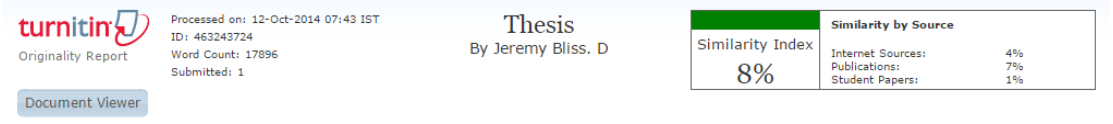
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I thank the almighty God for His grace and mercy in all the endeavors of my life. This study also I submit for the glory of His name.

I would like to express my sincere gratitude towards our principal, Dr. Alfred Job Daniel and the head of the department, Dr. Vernon Lee for all the freedom and opportunities they gave me; enabling me to complete this study.

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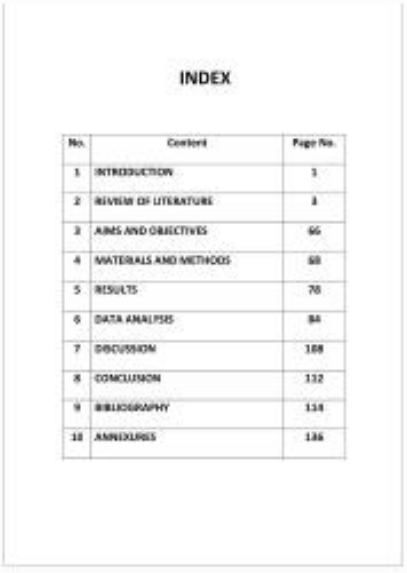

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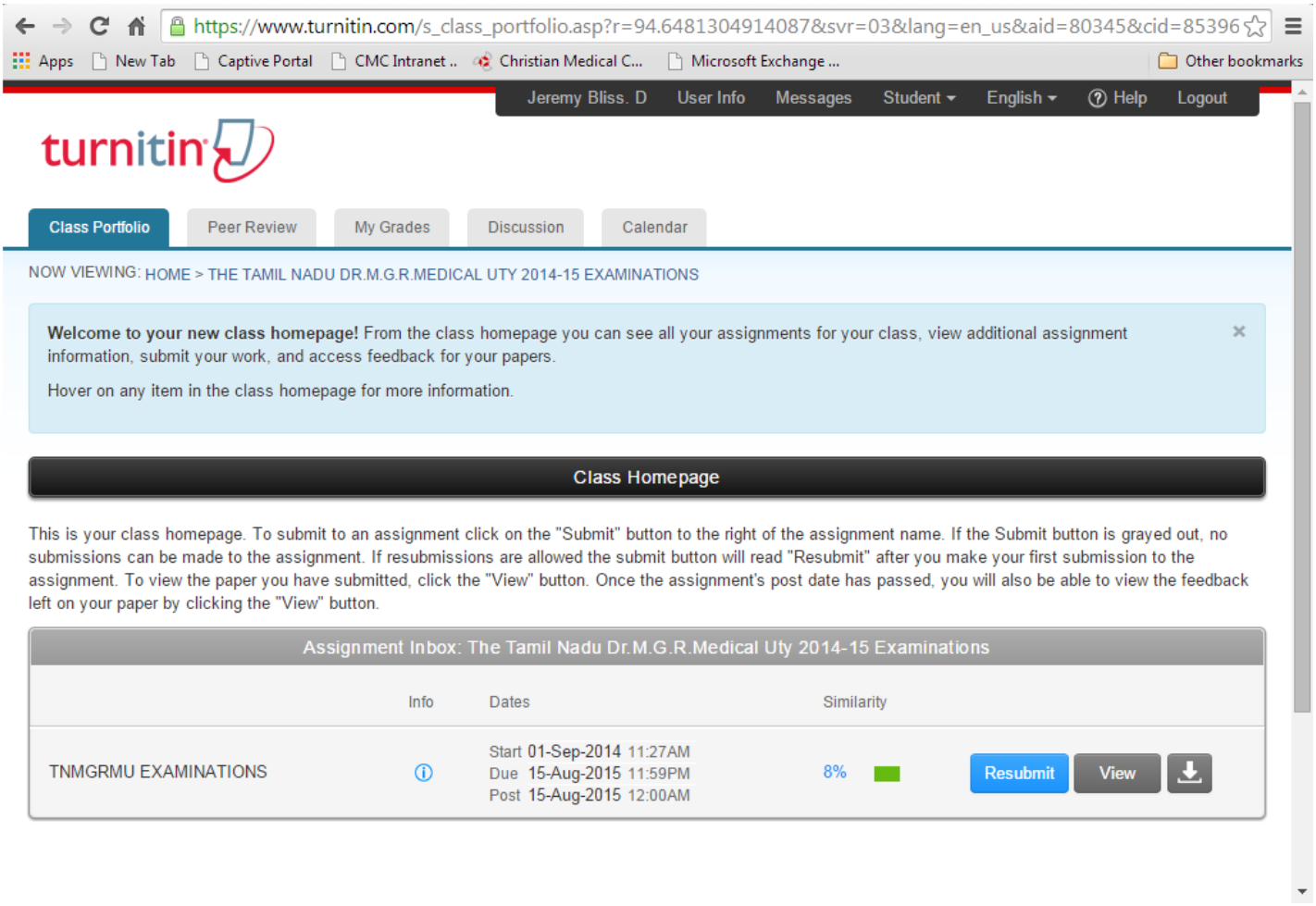
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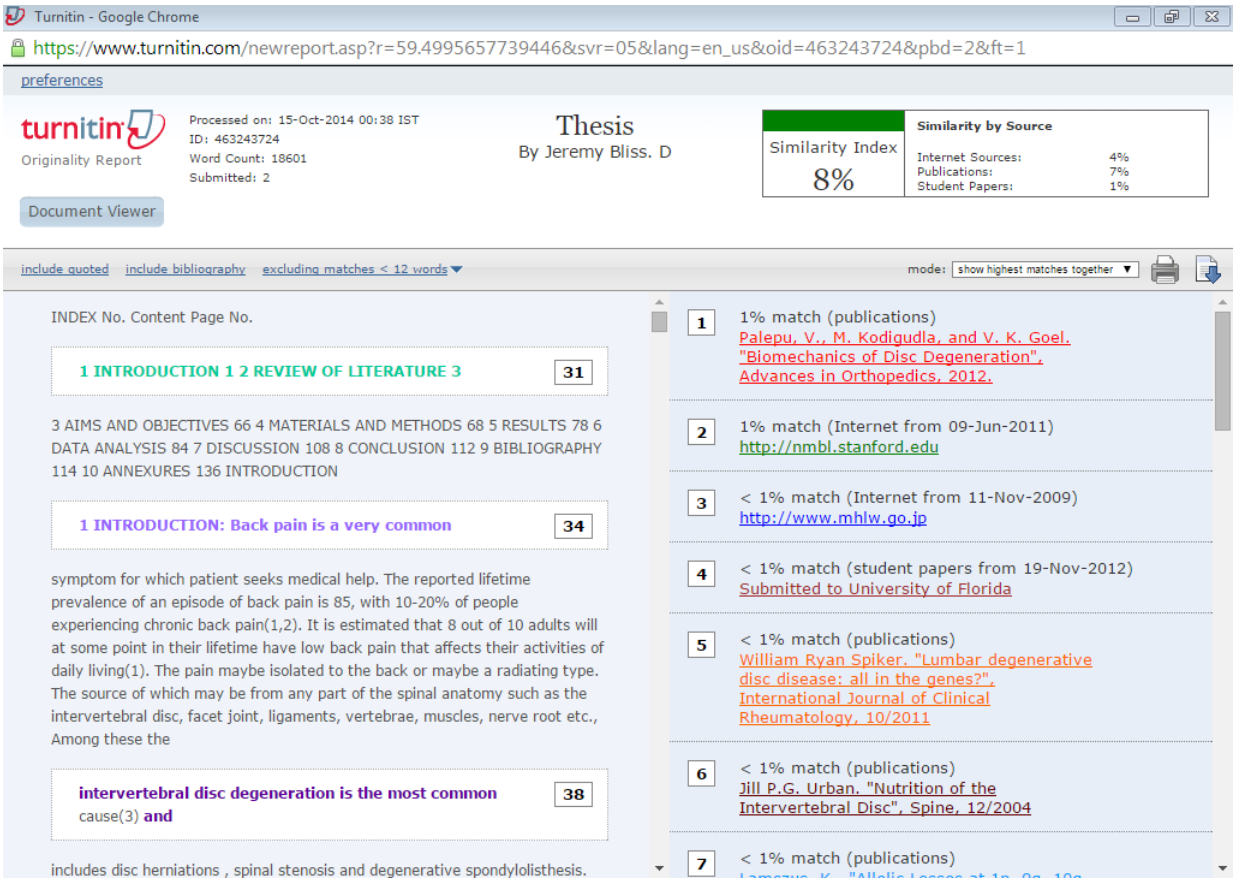
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1 INTRODUCTION: Back pain is a very common 34
symptom for which patient seeks medical help. The reported lifetime prevalence of an episode of back pain is 85, with 10-20% of people experiencing chronic back pain(1,2). It is estimated that 8 out of 10 adults will at some point in their lifetime have low back pain that affects their activities of daily living(1). The pain maybe isolated to the back or maybe a radiating type. The source of which may be from any part of the spinal anatomy such as the intervertebral disc, facet joint, ligaments, vertebrae, muscles, nerve root etc., Among these the
intervertebral disc degeneration is the most common 38
cause(3) and
includes disc herniations , spinal stenosis and degenerative spondylolisthesis.
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ABSTRACT

Title: ADJACENT SEGMENT DEGENERATION FOLLOWING SINGLE LEVEL FUSION AND SINGLE LEVEL DISCECTOMY – A COMPARATIVE STUDY

Department: Spinal Disorders Surgery Unit, Department of Orthopaedics

Name of Candidate: Dr. Jeremy Bliss D

Degree and Subject: Master of Surgery – Orthopaedics

Name of the Guide: Dr. Venkatesh K

OBJECTIVES: Determining Incidence of adjacent segment degeneration, its impact on the outcome after fusion and discectomy. Compare the two groups to understand the natural history of degeneration and influence of surgery.

METHODS: Patients who underwent single level instrumented posterior lumbar interbody fusion were evaluated with a minimum 2 year follow-up. The incidence of degeneration in the adjacent segment and the remaining lumbar segments were measured radiologically with Pfirrmanns, Bridwell, Fujiwara grading systems, functional outcome were measured with VAS, ODI, and JOA scoring systems, their relationship with certain patient risk factors like age, gender, BMI, co-morbidities, occupation and physiotherapy were checked. The findings were compared with a well matched control group of patients who underwent single level lumbar discectomy with the same follow-up criteria; they were also evaluated with the same parameters.

RESULTS: Adjacent segment degeneration occurs both in discectomy and single level fusion surgeries similarly, with the cephalic segment being affected more. There is no relationship between radiological degeneration and clinical outcome.

KEYWORDS: Adjacent segment degeneration, adjacent segment disease

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INTRODUCTION

INTRODUCTION:

Back pain is a very common symptom for which patient seeks medical help. The reported lifetime prevalence of an episode of back pain is 85, with 10-20% of people experiencing chronic back pain(1,2). It is estimated that 8 out of 10 adults will at some point in their lifetime have low back pain that affects their activities of daily living(1). The pain maybe isolated to the back or maybe a radiating type. The source of which may be from any part of the spinal anatomy such as the intervertebral disc, facet joint, ligaments, vertebrae, muscles, nerve root etc., Among these the intervertebral disc degeneration is the most common cause(3) and includes disc herniations , spinal stenosis and degenerative spondylolisthesis.

Spine related pain is treated with an aim of pain relief and not restoration of anatomy. Conservative treatment begins with oral analgesics and physiotherapy. Continuations of symptoms are managed with steroid injections or surgery. The conservative measures either decrease or modulate the inflammatory response but do not address the underlying pathology. Surgical treatment options are discectomy or spinal fusion; they provide pain relief but do not restore the load bearing capacity.

Source of back pain may be the disc, facet joints, nerve roots, vertebral body, ligaments and paraspinal muscles. 40% of back pain is related to the disc(4).

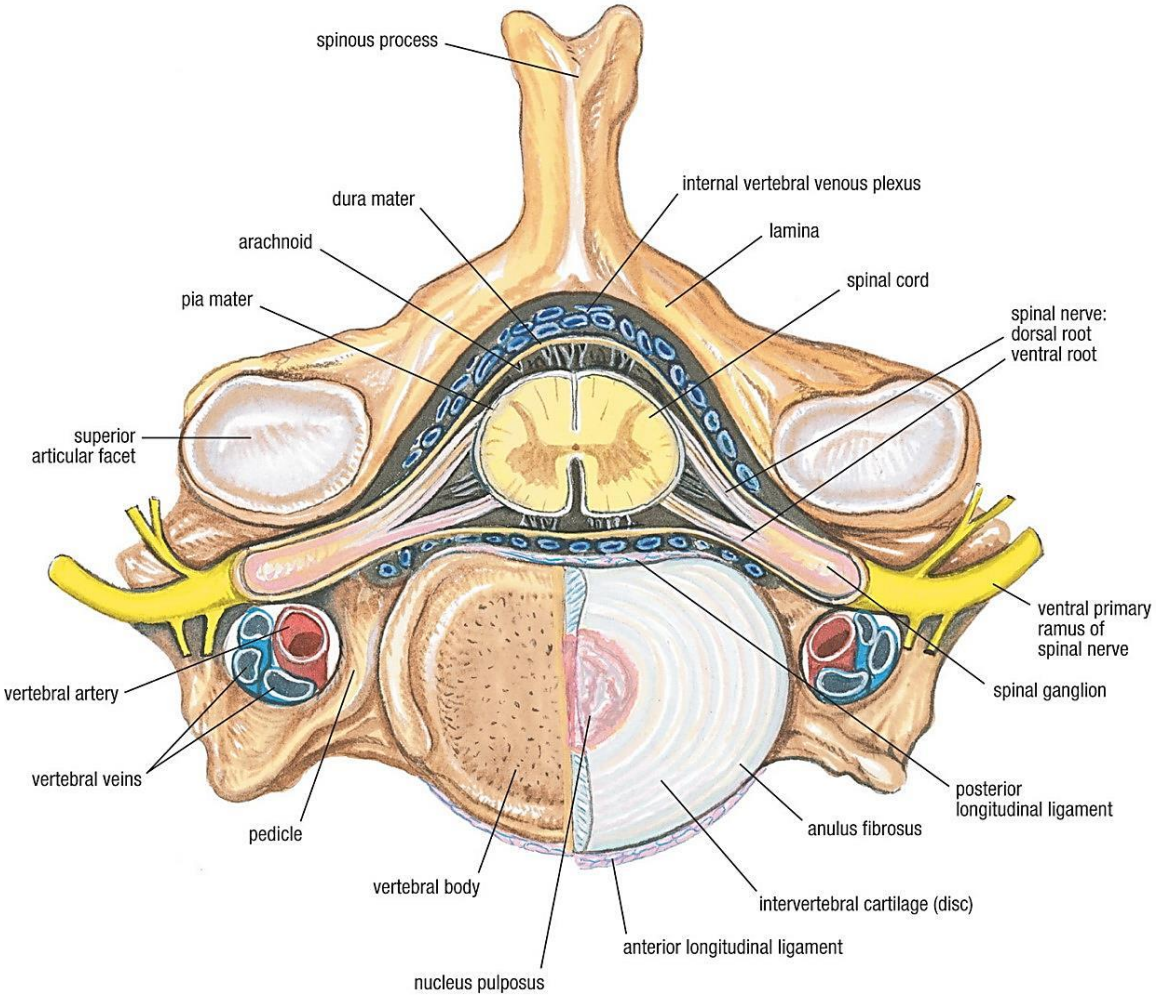
REVIEW OF LITERATURE

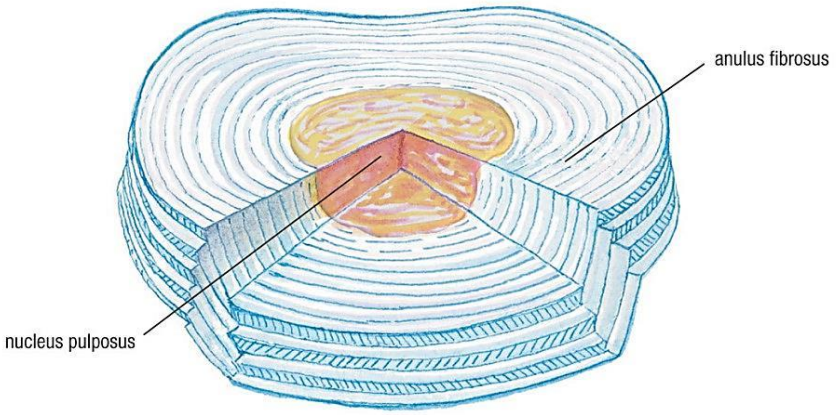
REVIEW OF LITERATURE:

Anatomy and Structure of the Intervertebral Disc:

The spinal column consists of 23 intervertebral discs separating24 vertebral bodies. The height and thickness of the disc vary according to the anatomical location of the individual discs. The discs have approximately 4cm Anteroposterior diameter and vary in height from 7 to 10mm(5), the thinnest discs are found in the thoracic region and the thickest in the lumbar region, sometimes up to 14mm in thickness(6). The total height of all the intervertebral discs, add up to one-third of the length of the spinal column. Together they provide mechanical functionality to the spine, including the transmission of axial loads between the vertebrae, transverse bending allowing lateral movement in the sagittal and coronal planes. It also provides flexibility to the spinal column for extension, flexion and torsion. More importantly, the mere presence of the intervertebral discs provides a dampening effect of the high-impact and high frequency events and thus absorbs mechanical energy(7).The Intervertebral discs are also called the diarthrodial joints of the spinal column since they function as articulations between the adjacent vertebrae(8).

VERTEBRAL AND INTERVERTEBRAL DISC ANATOMY





The intervertebral disc is composed of three parts:

i. cartilage end plates
ii. annulus fibrosus
iii. nucleus pulposus(7)

Each of these components has unique composition and function thereby ensuring a perfect biomechanically functioning intervertebral disc.

Cartilage Endplates:

Two thin layers of hyaline cartilage consisting of type II Collagen, glycosaminoglycans and water constitute the structure of the endplates. The endplates are approximately 1mm thick each and they sandwich the remaining disc material between them. They act as an interface between the vertebral body and the disc(7).

Histological analysis shows that the endplates are loosely attached to the vertebral bone by a thin layer of calcium(9) and not directly anchored to them through collagenous connections. The collagen fibers in the endplates run horizontal and parallel to the vertebral body and enter the disc(10). Chondrocytes are the main cells within a mature end plate and they are responsible for maintaining the collagenous matrix(11).

The dense fibers form the high collagen content of the endplates. They help in providing a strong barrier limiting the nucleus pulposus from protruding into the vertebra and also absorb the hydrostatic pressure and compressive stresses that

pass through the spine(12). The endplate also functions as a semi permeable membrane allowing movement of solutes between the discs and the vertebrae(13). The amount of water and proteoglycan content within the endplate regulate the diffusion of nutrients, the decrease in the proteoglycans influences the diffusion and is found to be associated with the degenerative loss of proteoglycans within the nucleus pulposus(14).

BASIC COMPONENTS OF THE IVD:

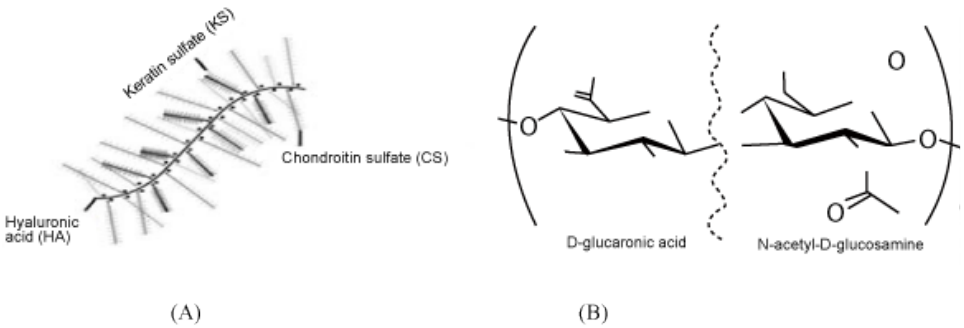
Components	Annulus Fibrosus	Nucleus Pulposus
Water	60-70 %, no change with age	90 % at birth
		80 % at age 20
		70 % at older age
Collagens (collagen I, collagen II, collagen X- collagen X is produced by the degenerated disc which has very poor mechanical properties)	Only collagen II, 50-60 % with (dry weight)	Only collagen I, 15-20 % with (dry weight)
	Little change with age	Little change with age
PGs (Proteoglycans)	15-20 % with (dry weight)	65% with (dry weight)
	Little change with age	Little change with age
Non- collagenous proteins and elastin	5-25% with (dry weight)	20-45% with (dry weight)
	Little change with age	Little change with age
Extracellular enzymes, age pigments, cells	Minor remainder	Minor remainder

Annulus Fibrosus:

It is a thick fibrous band restricting the nucleus pulposus and thereby determines the size and shape of the intervertebral disc. It has 15-25 layers of concentric lamellae composed of collagen type I (15,16). The adjacent layers of the collagen fibers within the lamella are parallel in 60° orientation alternating left and right to the vertical axis(11). The outer part of the annulus is attached to the anterior and posterior spinal ligaments and the vertebral bodies. The inner part is attached to

the endplates(7), through the radially passing elastin fibers which form Sharpey's fibers(17,18). This arrangement of the collagen and elastin fibers enables the annulus to resist the radial tension caused by axial loading; it functions as a limiting membrane like a capsule restraining the nucleus(7). The outer annulus cells are like fibroblasts and lie parallel to the collagen fibers; the inner cells are more oval. Some of these cells behave like mechanosensory cells having multiple long cytoplasmic projections(19,20).

It contains 65% of water; the rest of the dry content is made up of 55% collagen, 20% proteoglycan and 10% elastic fibers. Collagen Types I,II,III, V,VI and IX are present, the tougher Type I collagen is mostly seen in the outer annulus and the softer Type II Collagen is seen in the inner annulus. This arrangement allows compression under strain and recoiling to old shape after the strain is removed(21,22). The differentiation between the nucleus and annulus in an adult spine is not distinct. The annulus depends on the integrity of the nucleus to prevent the collapse of the lamellae inward(7).



A- A proteoglycan aggregate, B - Structure of hyaluronan

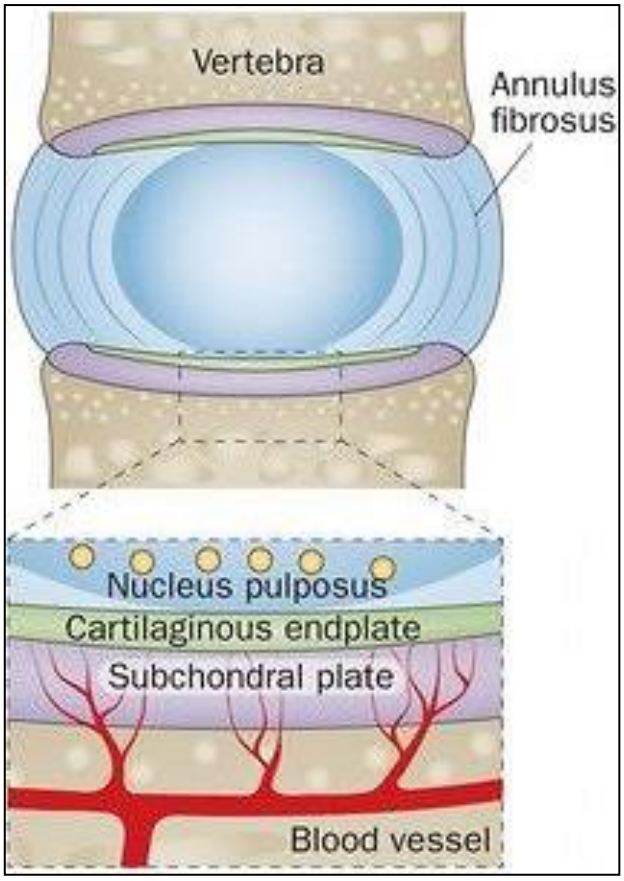
Nucleus Pulposus:

It is the semi gelatinous center of the intervertebral disc which is under hydrostatic compression(7). This well hydrated aggrecan rich gel contains two types of fibers, they are the radially arranged elastin fibers and the randomly organized collagen fibers(19,23). The nucleus pulposus is derived from the endoderm as a remnant of the notochord, in contrast to that of annulus and end plates which are from mesoderm. The cells are chondrocyte like and are responsible for the maintenance and repair of the nuclear matrix(24).

It is composed of 80% water; the rest of the dry matter is made up of 65% of proteoglycan, 17 % Type II collagen. Water is drawn into the nucleus by the negatively charged hydrophilic proteoglycans, therefore increasing the pressure allowing the disc to resist axial loading. The changes within the disc proteoglycan, influences the water content of the disc. Factors like age, disease and degeneration influence the proteoglycan content. Biochemical changes like nonenzymatic glycation, which occurs in aging and diabetes, also alter the proteoglycans(25,26). The disc hydration is also affected by the applied stress(27). The outer nucleus which is a transitional zone is regulated by chemical, hormonal and mechanical signals(28).

Anatomy of the Arterial supply to the Disc:

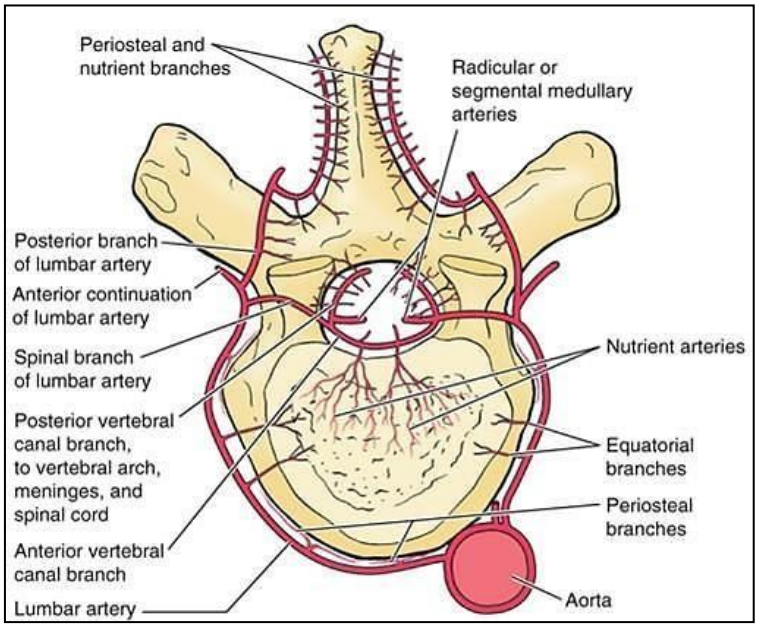
The blood supply for the vertebra starts from the aorta as segmental arteries; these vessels enter the vertebral body cross the marrow space and end as capillary buds at the cartilage end-plate–bone junction.



Normally four pairs of lumbar arteries from the aorta go behind the vertebral body and the fifth pair arises from the median sacral artery. These segmental arteries are called intercostals arteries in the thoracic region and as lumbar arteries in the lumbar region. These lumbar arteries are arranged longitudinally, forming loops both anteriorly and posteriorly. Each lumbar artery supplies the vertebral

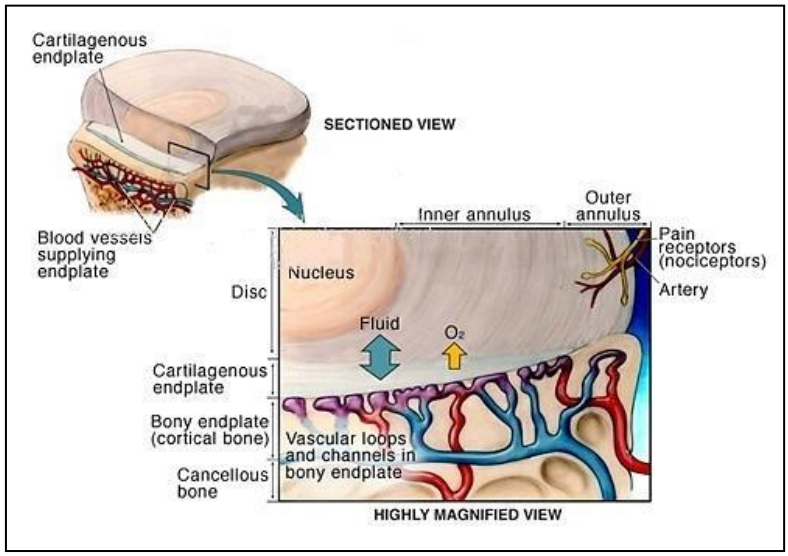
structures above and below the segmental level with anastamoses with adjacent segmental arteries. At the intervertebral foramen the lumbar artery divides into branches.

As the segmental arteries run along the anterolateral surfaces of the vertebral body, small branches of each segmental artery enter the vertebra. Along the sides of the vertebral body 10-20 periosteal arteries arise from the upper and lower surfaces of the lumbar artery. These periosteal vessels pass up and down the surface of the vertebral body and some of these cross the disc spaces through the peridiscal tissue and anastomose with their counterparts of the adjacent vertebrae. The main source of nutrition to the intervertebral disc comes from these marrow vessels that end as capillaries at the endplate. There are small branches on the discs, which penetrate the annulus fibrosus at its periphery and act as a source of nutrition to the outer disc.



Near the intervertebral foramen the segmental artery divides into two main branches. One branch goes posterior to supply the posterior vertebral processes. Another branch enters the spinal canal through the foramen along the spinal root and divides into dural and radicular artery. The segmental arteries supply blood to the structures inside and around the spinal canal at each segmental level(29,30).

The blood vessels that penetrate the subchondral bone to reach the surface of the endplate branch into capillaries. These capillaries that supply the disc eventually drain into the veins of the marrow spaces of the vertebral bodies. The arterioles have a sphincter at the base of the capillaries. These capillaries have muscaranic receptors that regulate blood flow in response to external signals; this mechanism may explain the decreased nutrient supply in response to smoking and vibration. Each capillary coils to form a microvessel loop called a vascular bud and each of these loops reassemble to form a venule. The venules form a network and enter the subchondral bone(31).

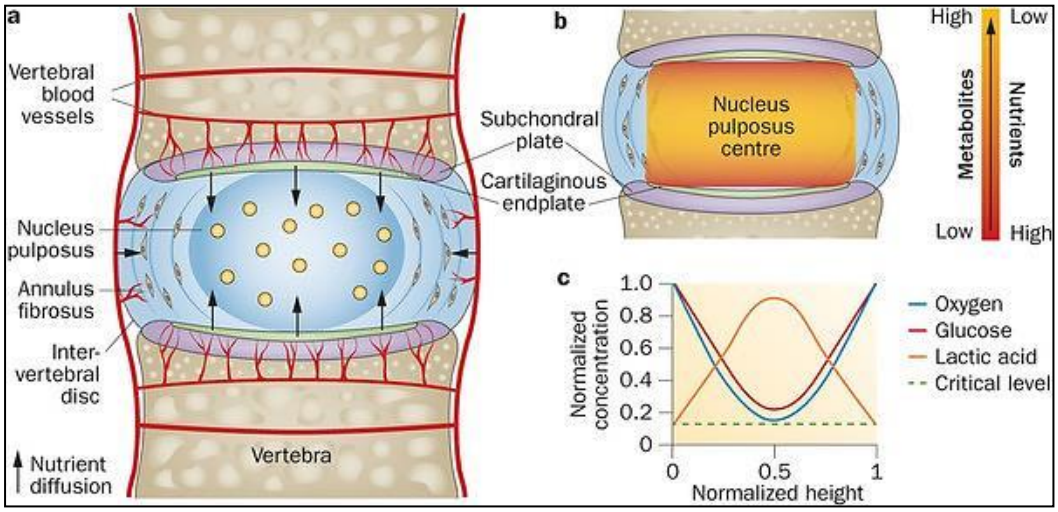


The shape of the vascular bud near the inner annulus is a simple loop-like structure, near the nucleus pulposus it is a swollen and complex coil like loop. The distance between each vascular bud is approximately 50micrometers, and there are about 16 vascular buds every 0.1mm² in both the inner annulus and the nucleus pulposus(31).

The density of the capillary bed is more in the central region of the disc and decreases toward the outer annulus. The density and integrity of these capillaries decreases with age. Any injury to the disc, sclerosis of the subchondral plate and mechanical environment affect the capillary bed architecture or the porosity of the subchondral plate, which eventually influences the delivery of nutrients to the intervertebral disc.

Nutrition of the Intervertebral Disc:

The intervertebral disc is avascular, so for it to remain healthy it requires nutrition which is mainly by diffusion which is dependent on the water content of the disc(11). In the first three decades of life there are tiny blood vessels in the endplates which supply nutrients to the endplates and the rest of the disc(7). These vessels gradually get disappear along with skeletal maturity, therefore making the intervertebral discs the largest avascular structures in the whole body(11).

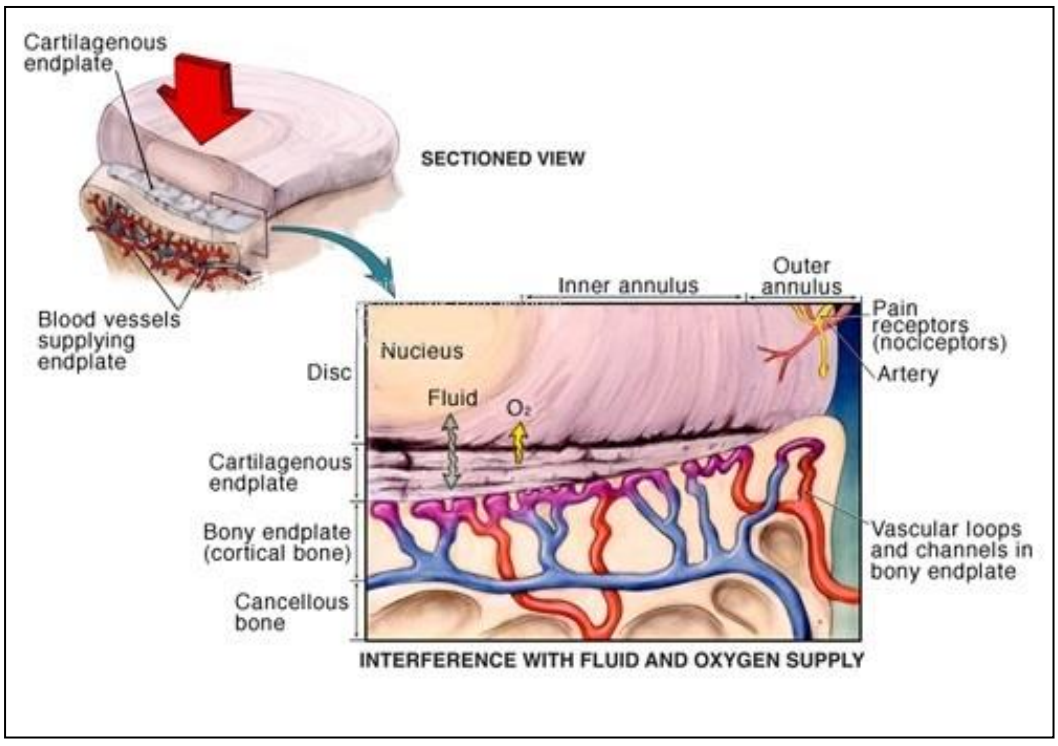


The two major pathways of nutrition to the intervertebral disc are:

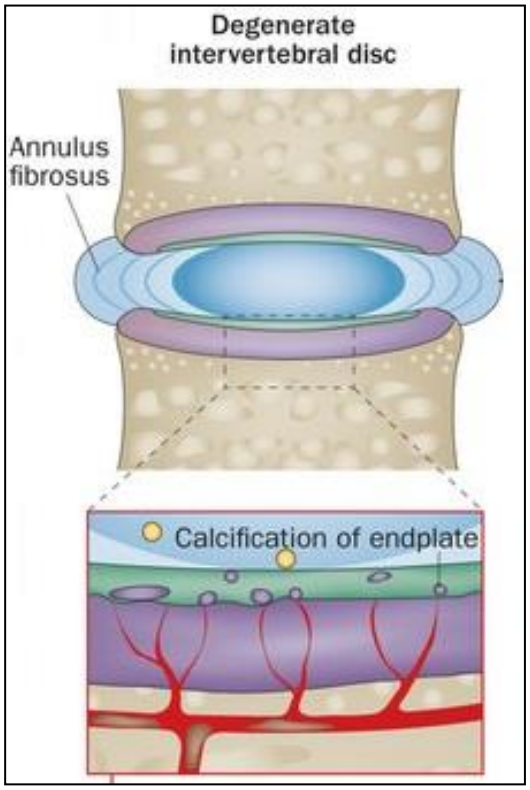
i. Diffusion across the endplate

ii. Through the small blood vessels of the outer annulus fibrosus.

The essential nutrients for the disc are glucose and oxygen, which are necessary for the survival and normal disc functioning. Other components like sulphates and amino acids which are required for the building of the proteoglycans transported through the vertebral blood vessels. The outer annulus derives nutrition from the nearby soft tissue like the longitudinal ligaments, whereas the inner annulus and nucleus depend on the diffusion of small nutrient molecules through the endplates from the outer annulus. The subchondral bone of the vertebral body has a capillary network which end at the endplate from where the nutrients diffuse across the endplates and then through the rest of the disc. Small uncharged molecules diffuse through the endplates and annulus to reach the center of the disc, while large molecules are excluded from the disc and positively charged molecules diffuse easily through the endplates(32,33).



The avascular disc is prone for age-dependent post-translational protein modifications like nonenzymatic glycation. They occur through amadori rearrangement of extracellular sugars forming the advanced glycation end-products (AGEs)(34). As age increases these AGEs tend to accumulate and influence the water retention capacity of tissues.



The nutrient supply of the disc is affected by molecular and structural changes within the disc. Normally the center of the disc has low glucose and low oxygen levels(35). Certain factors like calcification of the endplates, decrease in blood flow and decrease of proteoglycan synthesis influence the availability of nutrients. Lack of nutrients causes secretion of proteolytic enzymes causing cell death followed by degradation of the extracellular matrix(36–40).

Differences in the intervertebral discs of the cervical, thoracic and lumbar regions:

The difference in thickness of the intervertebral discs at various levels is associated with the function of balancing the range of movements and the mechanical load. The disc height is greatest in the lumbar region, followed by cervical and the least in the thoracic level(41). The caudal discs are capable of bearing the major load of the upper torso and the upper limbs, the larger disc allows more axial deformation and the increased cross-sectional area distributes the forces to decrease the overall stress(42).

The cervical and lumbar discs allow flexion, extension and lateral flexion; they are thicker in the anterior direction than in the posterior causing the lordotic curves. This feature is predominant in the fifth lumbar disc which is responsible for the lumbosacral angle. The lumbar discs allow less rotation compared to the cervical discs. Absence of disc and presence of horizontally oriented facet joints at the C1C2 level is the reason for maximum rotation around the odontoid. The cervical vertebrae transverse diameters are more than those of their intervertebral discs causing the edges of the vertebral bodies to almost overlap(43).

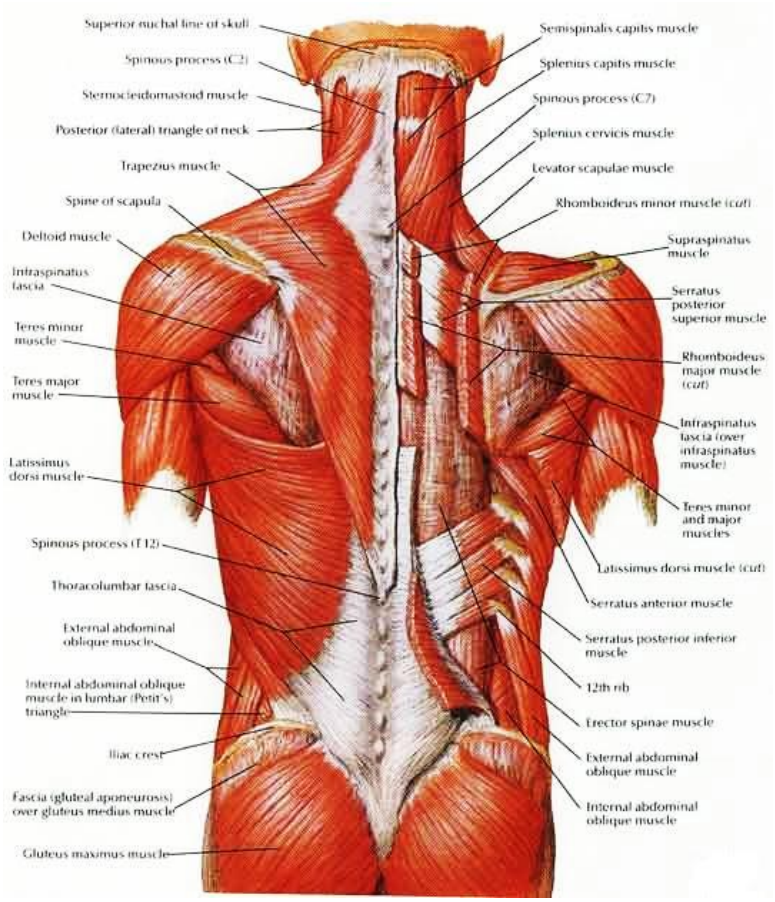
The movement in the thoracic spine is restricted owing to the presence of costovertebral joints, thereby increasing the stability to withstand axial loading(44). The rib cage and the sternum act as a barrel resisting flexion, extension and lateral flexion especially in the upper two thirds of the thoracic spine. The intervertebral

discs of the lower thoracic spine are thicker and allow increased mobility and ability to resist axial forces in comparison to the discs in the upper thoracic region(45).

ANATOMY OF THE SPINE MUSCULATURE:

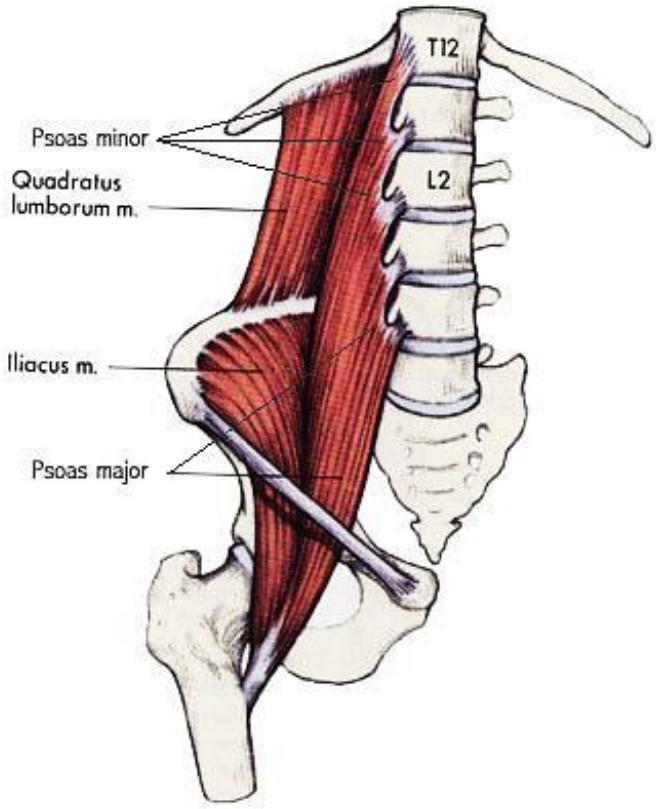
Muscles of the spine are an integral part of the movement and stability of the spine. They work in co-ordination with the vertebral column, ligaments and neural components and they prevent any excessive movement in one direction. They are divided into Intrinsic and extrinsic muscle groups. The Intrinsic muscles connect the vertebrae to each other and are innervated from the dorsal rami of spinal nerves and the extrinsic muscles connect the limbs to the vertebrae and they are innervated by the ventral rami of spinal nerves.

Extrinsic muscles of the back:



The muscles connecting the vertebral column to the shoulder are the trapezius, the latissmus dorsi, the levator scapulae, rhomboideus major and minor, the serratus posterior superior and serratus posterior inferior.

The muscles connecting the vertebral column and the pelvic girdle are the psoas major and the quadrates lumborum.

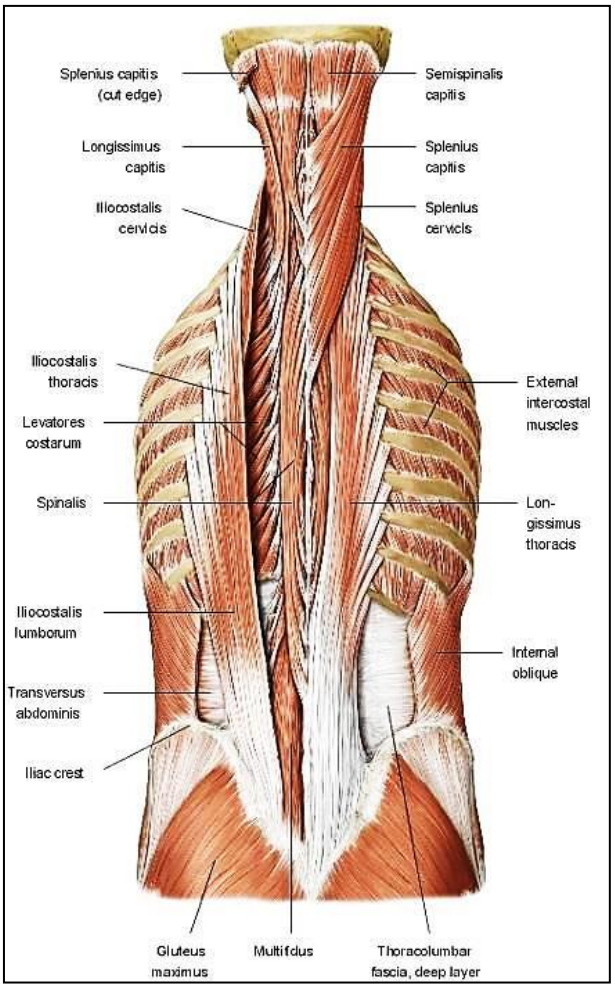


Intrinsic muscles of the back:

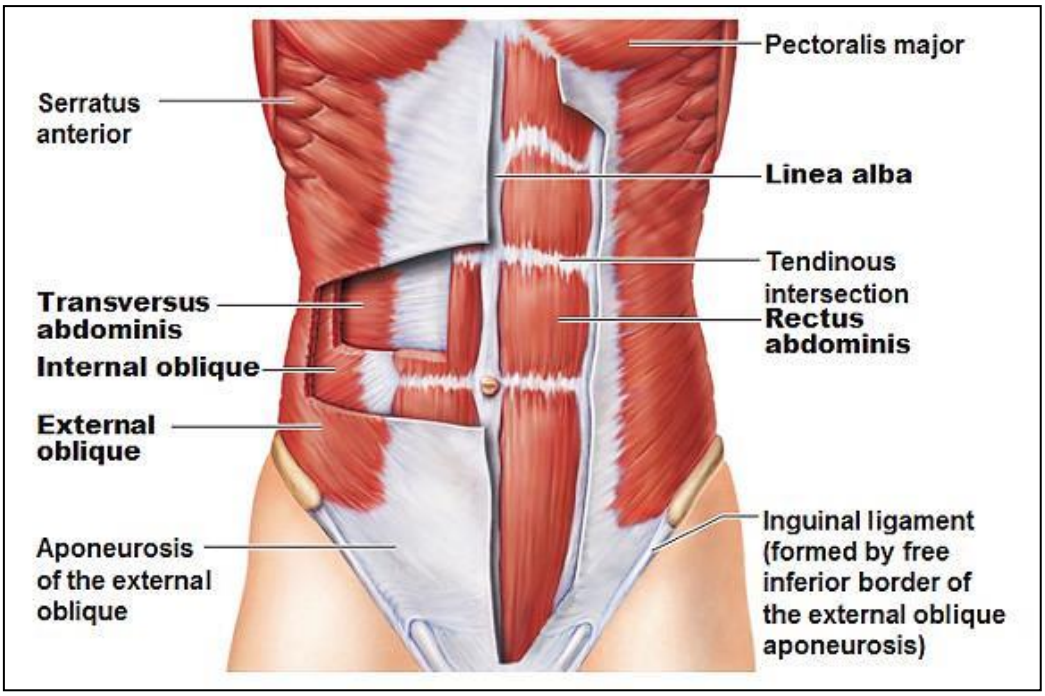
*Superficial Layer:*Consists of the erector spinae, which is the largest muscle mass in the back, it is well developed in the lumbar region and is known as the sacrospinalis. From lateral to medial this comprises three muscles: iliocostalis, longismus and the spinalis.

Intermediate layer: Consists of transversospinalis and multifidus muscles

Deep Layer: Consists of interspinalis and intertransversarii muscles.



Muscles that indirectly influence the spine are the External Oblique, Internal Oblique, Transversus abdominis, rectus abdominismuscles.



Function of the Spinal musculature:

Next to the vertebral column the muscles of the back are the most important structures of the back, playing a major role in the normal functioning of the spine. They help in all the range of movements and maintain the normal posture. They also function as shock absorbers. Their bulk protects the spine from the external forces.

The anterolateral abdominal muscles do not have direct attachment to the spine, but they aid in flexion, lateral flexion and rotation movements. They also help in maintaining posture and intra-abdominal pressure. These muscles especially recti

help in flexing the spine in a fixed pelvis. The external oblique rotates the trunk away from the side of contraction and internal oblique turns to the same side.

The spinal muscles are skeletal muscles and have a complex architecture; which is defined as the microscopic arrangement of the muscle fibers in relation to the axis of force generation(46), in other words it defines the muscle function. Three main types of muscle architecture are described:

i. Longitudinal: has fibers parallel to the axis of the force

ii. Unipennate: has fibers oriented at a single angle relative to the force axis.

iii. Multipennate: fibers oriented at several angles relative to the force axis.

Most of the back muscles are multipennate. They have very little tendon at their ends, there is a complex arrangement of internal tendons and aponeuroses. They have broad attachments, branch frequently and have multiple insertions at multiple vertebral levels. Some have short fascicles and high pennation, while others have long and parallel fascicles. The force generating and moment generating capacity depend on these factors, which in turn influences the control and mechanism of injury.

The length of the fascicle and the moment arm of the spinal muscles change with posture, for example; in the lumbar spine the function of the erector spinae changes with flexion. The line of action changes and therefore its capacity to resist

anterior shear forces is decreased, which is an important because the anterior shear loads are related to the risk of back injury(47).

Spinal Musculature dysfunction is hypothesized to cause segmental instability, low back and neck pain and disc degeneration. Chronic back pain patients show a selective decrease in extensor strength in comparison to flexors, back pain may inhibit neuromuscular function via nociceptive reflex feedback mechanism. Prolonged disuse and deconditioning causes muscle atrophy. Transverse abdominis muscle is the first muscle to be activated before the other spine muscles; it is found that in low back pain patients there is delay in its activation.When a skeletal muscle is suddenly lengthened when it is activated it results in muscle injury.

There are three ways of muscular injury:

i. The muscle itself may be injured because of eccentric contraction

ii. The muscle forces can alter the load distribution within the anatomic structures clinically linked to pain.

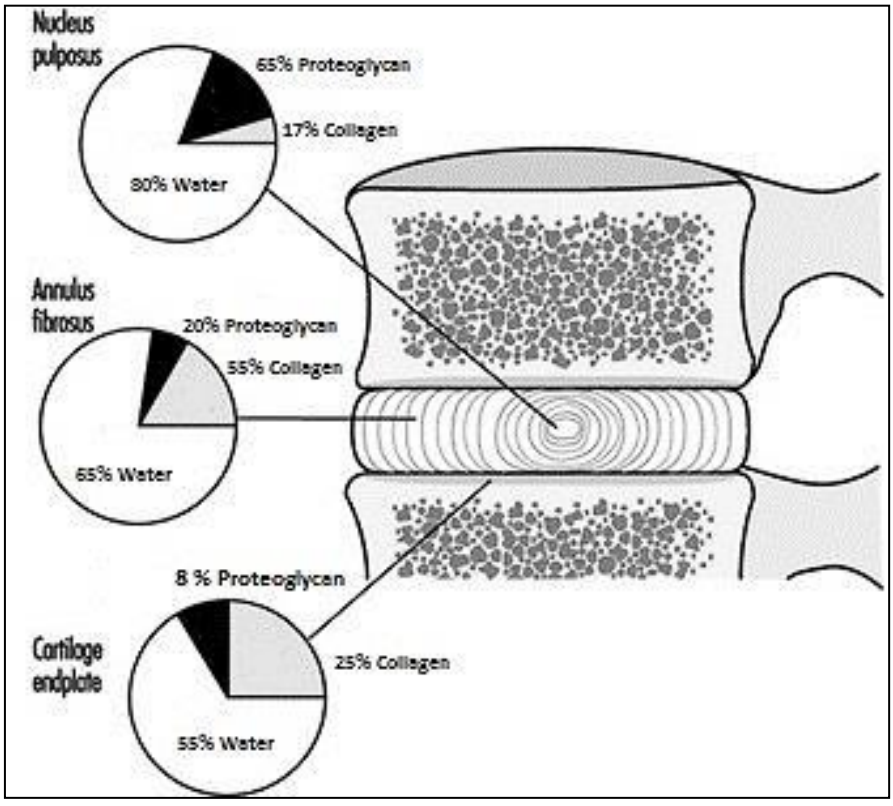
iii. Muscle activity can alter spinal stiffness and kinematics, which indirectly affect the load and strains on the soft tissue(48,49).

Muscle dysfunction destabilizes the spine, decreased the facet joint loading and increased the load on the disc and ligaments(50).

PATHOPHYSIOLOGY OF DISC DEGENERATION:

With aging and degeneration, the intervertebral disc is transformed from an efficient shock absorber, which is capable of withstanding increased loads into an incompetent fibrous tissue prone for cracks and fissuring which result in various clinical disorders.

The embryonic spine is formed from central notochord and the surrounding mesoderm, the nucleus pulposus arises from the notochord and the annulus fibrosus from the mesoderm. The different embryological origins explain some of the differences in structure, organization and biochemical composition between the nucleus and the annulus(51).



The two major proteins that form the intervertebral disc are the collagen and the proteoglycans. The main function of the collagen is to provide tensile strength to the disc. Type I collagen is abundant in the annulus fibrosus and is responsible for the tough fibrous nature. Type II collagen is abundant in the nucleus pulposus and is responsible for its more malleable nature.

Proteoglycans are a type of glycoprotein made up of glycosaminoglycans (GAG), the most common of which is Aggrecan. This aggrecan is composed of chondroitin-6 sulfate and keratin sulfate side chains which are bound to a core protein. These large highly charged aggrecan molecules have water binding capacity because of their negative charge and the hydrophilic nature. The nucleus pulposus cells produce large amount of these proteoglycans and aggrecan, enabling it to draw in water and maintain the gel like consistency which provides the compressive cushion effect. The annulus cells also produce proteoglycans. Proteoglycans also affects the permeability and diffusion rates of the intervertebral discs(52).

Growth Factors:

The development, regulation and degeneration of the intervertebral discs are influenced by several growth factors. Each of them has different effect on the nucleus pulposus and the annulus fibrosus depending on the stage of development or degeneration. BMP-2, OP-1, insulin growth factor-1(IGF-1), fibroblast growth factor (FGF) and IL-1 are some of the important growth factors in this regard(53–58).

Bone morphogenic proteins are multifunctional growth factors belonging to the TGF-beta family and maybe involved in the homeostasis of the intervertebral disc. Recombinant BMP-2 stimulates the expression of a chondrocyte phenotype in the disc cells and also cause up regulation of aggrecan, collagen I and collagen II mRNA. Osteogenic protein-1(OP-1/BMP-7) and insulin growth factor-1(IGF-1) are other factors which produce proteoglycans. Basic FGF is an important regulator of proteoglycan metabolism and cartilage homeostasis by acting as a pro-catabolic agent and anti-anabolic mediator(59–62).

IL-1 is a pro-inflammatory cytokine contributing to the loss of matrix homeostasis by inhibiting aggrecan synthesis(63), it plays a catabolic role and increases proteoglycan degradation and stimulates production of matrix metalloproteins, nitric oxide and prostaglandin E2 by the disc cells(64–66).

Mechanism of Disc Degeneration:

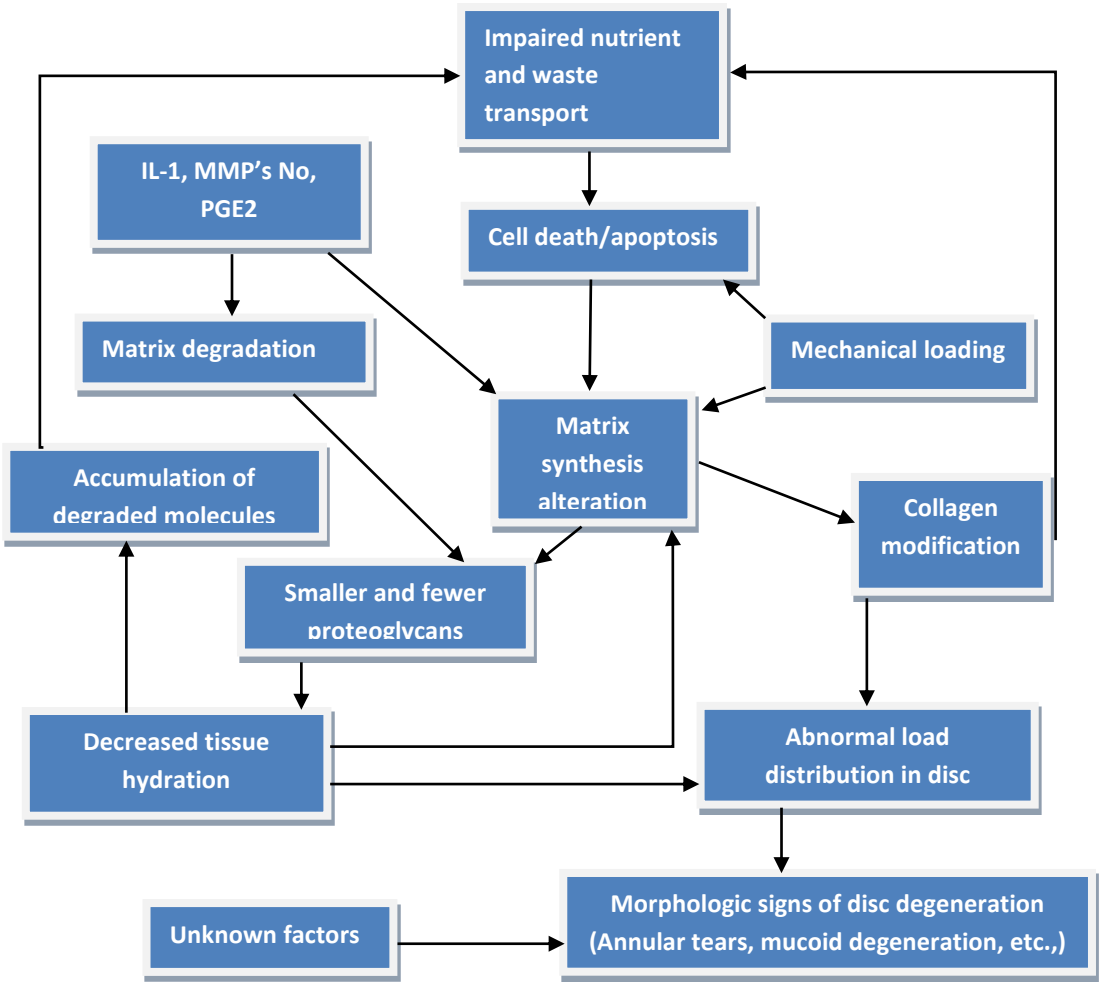
Homeostasis of intervertebral disc:

The cells of the nucleus and the annulus regulate homeostasis through cytokines, enzymes, enzyme inhibitors and growth factors(53,57). Degeneration of the disc may occur due to the imbalance between the anabolic and catabolic processes(67).Pro-inflammatory cytokines, expression of matrix-degrading enzymes including matrix metalloproteinases, aggrecanases and growth factors are associated with disc degeneration(64).

Microscopic degeneration:

The ratio of Type I to Type II collagen changes with age, increasing the fibrous type I collagen in both the nucleus and the annulus(68). The collagen fibers themselves get altered by proteolytic cleavage of collagenases and nonenzymatic cross linking of collagen, which change the mechanical properties of the cells of the disc(69).

Loss of aggrecan is another factor, with increasing age there is decreased production of proteoglycans, therefore less aggrecan(70–72). The chondroitin sulfates in the side chains of the glycosaminoglycans are replaced by keratin sulfate(73). These changes decrease the water holding capacity of the disc.



Microscopic Disc Degeneration Cascade

The loss of Type II collagen and aggrecan decreases the ability of the disc to compress and swell. The various microscopic changes in the proteoglycans and the collagen gradually starve the disc off its nutrition. Added to this the cell viability and synthetic capacity decrease with age resulting in cell loss through apoptosis and Fas-mediated mitochondrial caspase-9 pathway(39,74,75). Therefore the overall disruption of homeostasis, decreased nutrition, cell changes and apoptosis accounts for the microscopic degeneration of the disc.

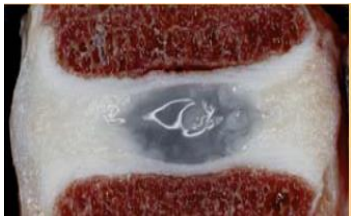
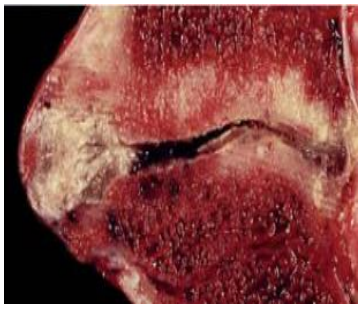
Macroscopic Degeneration:

All the changes in the microscopic level together create the macroscopic changes, the inflow and outflow of water which is the basis of the creep phenomenon in a normal disc is hampered in a degenerated disc. This alters the deforming capacity of the disc and slows down the recoiling character when the load is removed(76).

Uneven stress distribution and repetitive loading cause local trauma; which is not repaired properly by the aging disc(77).Multiple such localized trauma, decreased turnover and synthetic rate of the disc cells progressively weaken the disc, making it vulnerable to further injury. Fissures and radial tears can develop in the annulus and further loading of the weakened disc ultimately leads to herniations of the nucleus. As a result a marginal instability starts within the spinal units, and these biomechanical changes result in biochemical changes within the disc. The load now shifts to the posterior elements, overloading the facet joints and increase the demand on the musculoskeletal tissues also.

By the third decade of life the blood supply to the center of the disc effectively recedes, making the disc depend mainly on diffusion for nutrition. And with age the endplates calcify causing hindrance to the diffusion(78). The combination of altered biomechanics and compromised blood supply results in a acellular, avascular disc with decreased potential for self-repair.

Age related disc degeneration-Thompsons grading

Grade I: normal juvenile disc • nucleus pulposus and anulus fibrosus can clearly be distinguished • the nucleus pulposus has a gel-like appearance and is highly hydrated • anulus fibrosus consists of discrete fibrous lamellae • cartilage endplates are uniformly thick and consist of hyaline cartilage	
Grade II: normal adult disc • peripheral appearance of white, fibrous tissue in the nucleus pulposus • mucinous material is found between the lamellae of the anulus fibrosus • thickness of the cartilage endplate is irregular	
Grade III: early stage • consolidated fibrous tissue in the whole nucleus pulposus • demarcation between nucleus pulposus and anulus fibrosus is lost and extensive mucinous infiltration in the anulus fibrosus is observed • cartilage endplates show focal defects	
Grade IV: advanced stage • clefts in the nucleus pulposus appear, usually parallel to the endplate • focal disruptions are found in the anulus fibrosus • hyaline cartilage of the endplate is replaced by fibrocartilage; irregularities and focal sclerosis are found in the subchondral bone	
Grade V: end stage • typical disc structure may be lost completely • clefts extend through nucleus pulposus and anulus fibrosus • endplates display diffuse sclerosis	

GENETICS OF DISC DEGENERATION:

Genetic Influence:

Monozygotic twin studies have shown that there is 29-54% genetic influence for the disc degeneration seen(79). Disc herniations are found to be more in patients with a similar family history. Such twin studies had the disadvantage that they have similar environmental exposures and recall bias. In another observation eliminating these bias it was revealed that genetic influence was seen, both in near relatives with similar environmental exposures and in distant relatives who had different environmental exposures(80).

Associated genes:

In 1998 Videman at al found that TaqI and FokI of the vitamin D receptor gene were associated with disc bulging, decreased MRI signal intensity and decreased disc height(81). Genes encoding type-IX collagen, type-XI collagen, cartilage intermediate layer protein, aggrecan and MMP-2 and other disc proteins have association with disc degeneration (82–86). Gender and ethnic differences may play a role in the genes responsible for disc degeneration.

The role of structural, degenerative and inflammatory genes was shown in a study which correlated the MRI findings and the genetic data, evaluating aggrecan

gene, 12 collagen genes, 8 interleukin genes and 4 matrix metalloproteinase genes. They were found to be associated with the radiographic degeneration(87).

The theory of chronic pain condition being related to disc disease more than biomechanical problems have been proposed by some quoting the variation in symptoms in individuals with radiographic disc degeneration. Catechol-O-methyltransferase(COMT) encodes an enzyme which is important for the breakdown of pain – causing neurotransmitters dopamine and epinephrine. Variations in COMT allele have been linked with post-operative outcomes in patients with lumbar disc degeneration; homozygotes experience better improvement than heterozygotes(88).

Genes associated with Disc Disease	
Gene Category	**Examples**
Vitamin D Receptor	FokI and TaqI
Aggrecan	ACAN
Collagen	COL1, COL9, COL11
Cartilage	CILP
Interleukin	IL1, IL6, IL10, IL18
Matrix metalloproteinase	MMP1, MMP2, MMP3, MMP9

The GCH1 gene encodes a protein in nitric oxide synthesis. Nitric oxide synthesis is involved in pain transduction. A single nucleotide polymorphism (SNP) within the gene was associated with significant improvement in functional outcome and pain in patients with disc degeneration. The regenerative effects of the proteins associated with disc degeneration have been seen in animal and human models(55). The role of collagen variants and extracellular matrix components on the disc degeneration, if understood better will lead to improved diagnosis and treatment of disc degeneration.

ROLE OF INFLAMMATION:

INFLAMMATION IN DISC DEGENERATION:

Spine degeneration is progressive and can be related to the initiation and propagation of anti-inflammatory cascade.

Inflammatory mediated pain

As the disc degeneration progresses the tears in the annulus fibrosus triggers ingrowth of blood vessels and nociceptors into the outer and inner annulus. Pain is caused when these nociceptors and the cytokine signals of the inflammatory mediators are stimulated.

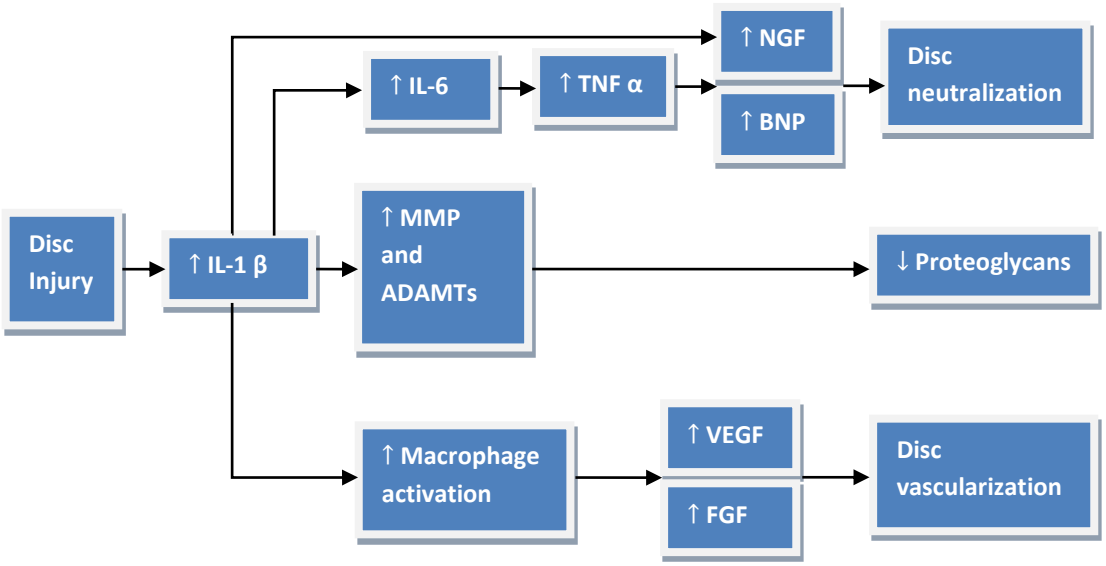
Inflammatory molecules involved in disc degeneration	
IL-1β	Interleukin 1 beta
TNFα	Tumor necrosis factor alpha
IL-6	Interleukin 6
iNOS	Inducible nitric oxide synthase
PGE2	Prostaglandin 2
MMP	Matrix metalloproteinases
ADAMTS	A disintegrin-like and metalloprotease with thrombospondin Type 1 motifs

Pain response is triggered by inflammatory mediators through many biochemical pathways and symptomatic patients have inflammatory mediators which are not present in asymptomatic patients, for example Interferon gamma(89), interleukin I beta and tumour necrosis factor alpha. These findings show that there is a connection between inflammation and back pain, probably this is the reason why some patients with less radiographic disc degeneration have pain while others with more radiographic degeneration have less symptoms.

Pathogenesis of Inflammatory Cascade

With aging disc degeneration progresses due to the decrease in disc water content which is a result of the decreased proteoglycans and collagen content. These changes initiate the inflammatory cascade which in turn aggravate the proteoglycan deficiency and disorganize the endplate articular cartilage matrix(90).

The major proteoglycan and collagen degradative enzymes responsible for disc degeneration are the matrix metalloproteinase (MMP) and ADAMT (a disintegrin and metalloproteinase with thrombospondin motifs)(91). They are produced by chondrocyte like cells in the nucleus and inner annulus, and they are regulated by inhibitors of metalloproteinase (TIMP). Dysregulation of MMPs, ADAMTs and TIMPs result in catabolism.



Inflammatory response to disc degeneration

Intervertebral disc cells in response to disc injury produce inflammatory mediators like interleukin 1β and TNFα. IL-1β increases the matrix metalloproteinase 2 (MMP-3), MMP-13 and ADAMTS-4 and decrease the genes for matrix homeostasis-aggrecan, collagen II and collagen I), it also induces nitric oxide (NO), interleukin 6 (IL-6) and prostaglandin E2 (PGE2). IL-6 decreases collagen and aggrecan and proteoglycan synthesis and increases MMP-3 and TNFα(92,93).

TNFα decreases gene for aggrecan and Type II collagen and increases the gene for MMP-1, MMP-3, MMP-13, ADAMTS-4 and ADAMTS-5. It also stimulates IL-6, IL-8 and PGE2(94,95).

Response to inflammatory cascade

Disc injuries like annular tear change the histology of the disc, in the form of vascularized granulation tissue along the tears. This granulation tissue extends through the annulus into the nucleus(96,97). They contain vascular endothelial growth factor (VEGF), fibroblast growth factor (FGF) and transforming growth factor 1β (TGF-1β) which is not seen in normal discs. The new vascularization of the disc brings macrophages and mast cells as an additive to the inflammatory cytokines(97). These macrophages apart from their own catabolic activity they also increase the expression of the inflammatory cytokines like IL-6 and IL-8(98).

Along with the angiogensis neurogenesis also happens. IL-1β and TNFα are released by the injured annular cells which increase the nerve growth factor (NGF) and brain-derived neuropathic factor (BNP) in the nucleus(99); they in turn induce formation of sensory axons and nociceptive sensory neurons. These new innervations contribute to the discogenic pain(97,100). NGF also sensitizes nociceptors and the inflammatory mediators irritate the new nerve endings, both causing increase in pain.

Catabolic proteins involved in disc degeneration	
Catabolic protein	**Inhibitor**
IL-1β	IL-1 receptor antagonist (IL1-Ra)
TNFα	TNFα monoclonal antibody
IL-6	IL-6 receptor antibody
MMP	Tissue inhibitors of metalloproteinases (TIMP)
ADAMTs	Tissue inhibitors of metalloproteinases (TIMP)
PGE2	Cyclooxygenase (COX) inhibitor

Treatment for disc pain should be targeted on the major inflammatory cytokines and mediators. IL-1β is the significant disruptor of the homeostatic balance and so inhibitors of IL-1β produce an overall suppression of the inflammatory response.

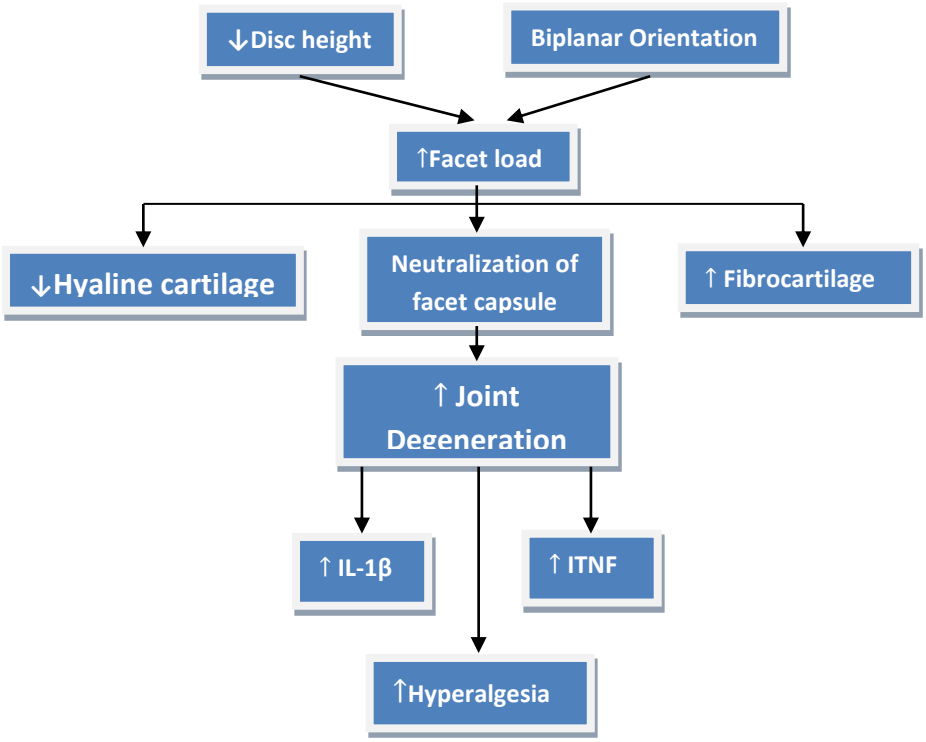
INFLAMMATION IN FACET JOINTS

The facet joint is a zygoaphophyseal joint made up of both inferior articular facet of the superior vertebra and superior articular facet of the inferior vertebra. The joint is lined by hyaline cartilage and covered by fibrous capsule with synovial fluid inside. The cartilage is made up of water, type II collagen, chondrocytes and extracellular matrix.

The synovial fluid is produced by two types of synovial cells lining the joint, Type-A cells are like macrophage and Type-B cells are like fibroblasts. The synovial macrophages initiate their inflammatory response only when the joint is damaged. They release IL-1β and TGFα, which in turn stimulate angiogenesis, leukocyte and lymphocyte recruitment, fibroblast proliferation, IL-6, IL-8, protease and prostaglandin secretion. These macrophages also interact with T cells which increase proinflammatory mediators like IL-1α, IL1β, TGFα and MMPs(101,102). The synovial macrophages are found more in affected patients; therefore these synovial macrophages are good targets for biological therapy to reduce inflammation.

Chronic overload of the facet joints results in arthritic changes and the orientation of the joint line becomes coronal(103). This increases the biomechanical stress on both the disc and the facet joints which induces the inflammatory cascade(104).

The increased load on the facet joint which induces the inflammatory cascade eventually causes the hyaline cartilage to change to fibrocartilage in the joint surface. The fibrocartilage is prone for more degeneration on loading(105). Together the articular cartilage loss, capsule redundancy and degeneration of the joint finally lead to spondylolisthesis.



Inflammatory response of facet joint degeneration

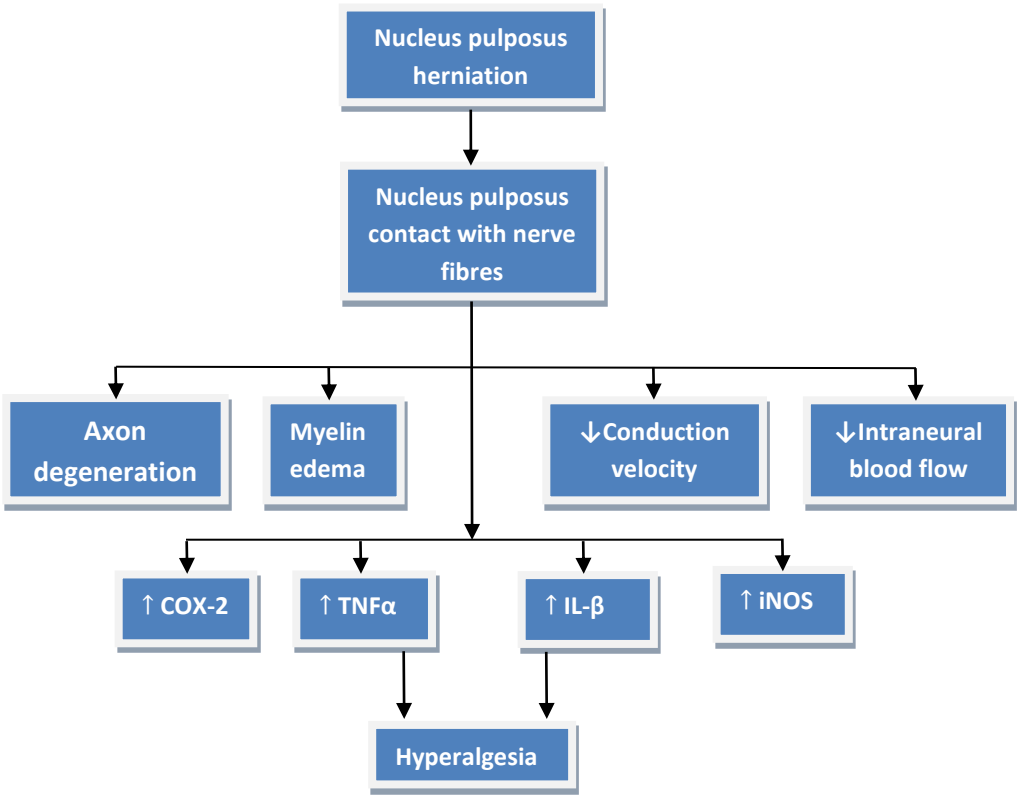
As in the intervertebral disc there is angiogenesis and neurogenesis which occur in the facet joint articular cartilage which is normally avascular. The vessels and nerve fibers travel from the subchondral bone to the articular cartilage(106). IL-1β and TNFα sensitize the nerve fibers resulting in hyperalgesia. IL-1β is highly

concentrated in the facet joint capsule in symptomatic patients compared to asymptomatic patients(107). Animal experiments with IL-1β receptor antagonists have shown that MMPs decrease resulting in chondroprotective effect(108).

Inflammation in Central and Peripheral Neural structures:

Peripheral Radiculopathy:

Radicular pain occurs as a result of nerve root compression due to disc herniations or nerve root irritation. The nerve root irritation could be the reason why many symptomatic patients do not have corresponding radiographic findings. The relief of symptoms for such patients with NSAIDS may be explained by an inflammatory cause for the radiculopathy(109).



Inflammatory response disc herniation

Disc herniations expose the nerve roots to the inflammatory factors of the nucleus, which decreases the nerve conduction velocity and hyperalgesia. It also causes axonal degeneration, decreased intraneural blood flow, intravascular coagulation and myelin edema(110–113).TNFα causes Schwann cell injury, nerve edema, myelin splitting and fibroblast and macrophage activation of the peripheral nerves and nerve roots(111,114). TNFα, IL-1β, inducible nitric oxide synthase (iNOS) and cyclooxygenase 2 (COX-2) also play important role in radicular pain following compression(115). The herniations of the nucleus and nerve root displacement together induce more pain than individually(116).

Nerve root compression causes damage to nerve fibers decreasing blood flow and increasing vascular permeability due to disruption of the blood nerve barrier of the intraradicular vessels. There is increase in endoneurial pressure and subsequently nerve damage(111). Once the myelin sheath is disrupted the T-cells which lie within the nerve roots release IFN-I and macrophage activating molecules, following which the macrophages infiltrate and phagocytize the damaged tissues. The macrophages release TNFα and IL-1β which also irritate the nerve root.

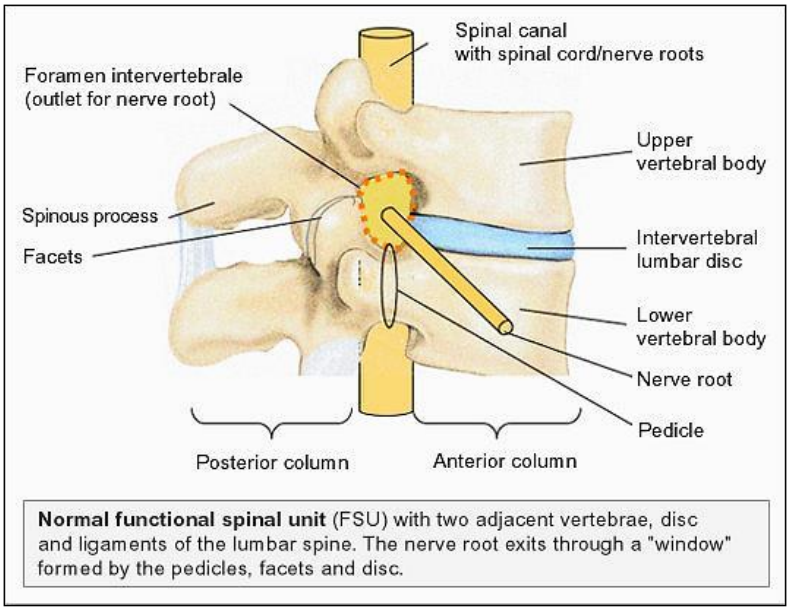
Spinal stenosis:

Spinal stenosis is seen in spondylolisthesis, ligamentum flavum thickening, vertebral osteophytes, bulging discs and hypertrophied facet joint(117). Narrowing of the central canal, lateral recesses or neural foramina result in neural compression. Movement affects the space within the canal; extension decreases central and

foraminal area and also decreased midsagittal and subarticular sagittal diameters, the opposite happen in flexion(118). So the patient adopts a forward leaning stance since they are symptomatic in spinal extension.

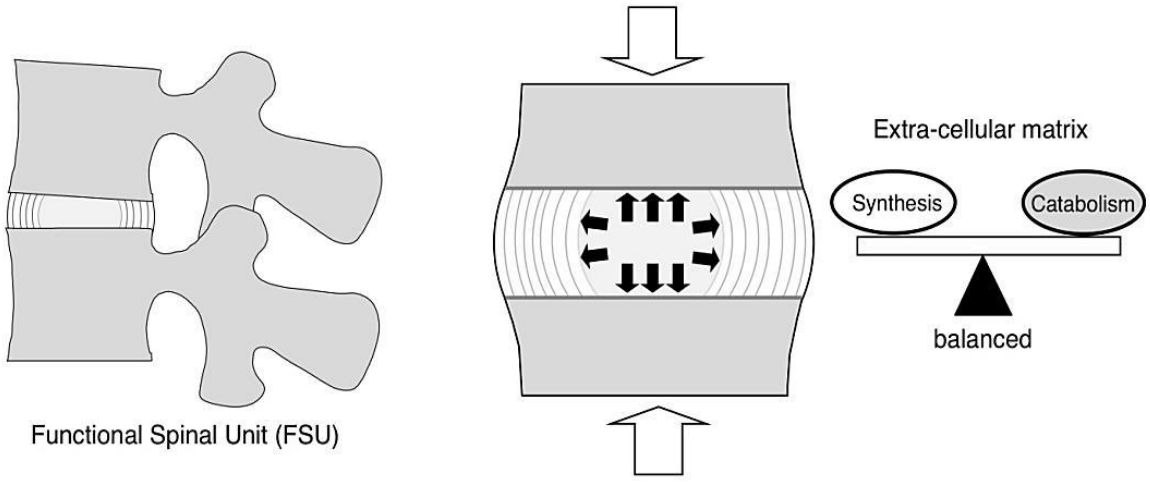
With aging the ligamentum flavum becomes thicker and less elastic, the elastic fibers are replaced with Type-I collagen. The mesenchymal stem cells and fibroblasts in the ligamentum flavum release TGF-β influencing the inflammatory cytokines(119,120).

BIOMECHANICS OF NORMAL INTERVERTEBRAL DISC:

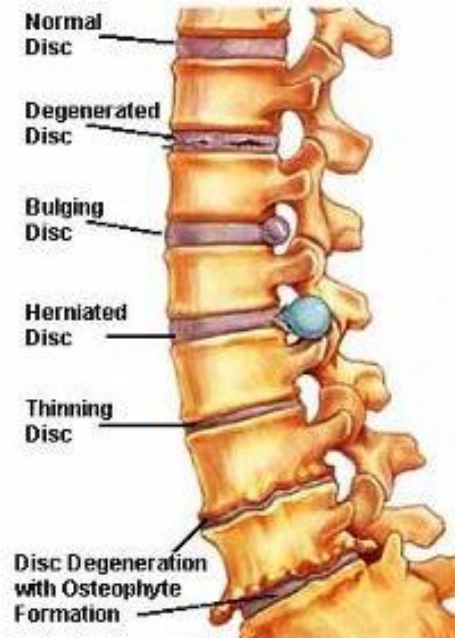


Normal functional spinal unit (FSU) with two adjacent vertebrae, disc and ligaments of the lumbar spine. The nerve root exits through a "window" formed by the pedicles, facets and disc.

A functional spinal unit is one which is composed of two adjacent vertebrae, the intervertebral disc in-between, superior and inferior facet joints and the connecting ligaments. The spinal unit allows multiaxial movement and loading of the spine and also distributes the stress from both axial and eccentric compression forces(121). The intervertebral disc is responsible for the load bearing, shock absorption and mobility between vertebrae. The facet joints are true synovial joints. The intervertebral disc is a major contributor to the biomechanics of the spine. The disc has the capacity to resist anterior and lateral shears and compression therefore making it an important weight bearing part of the spine(122). Disc degeneration is associated with normal aging, it can also occur due to other reasons like mechanical factors causing structural damage in the form of annulus tears, disc prolapse, internal disruption, end plate damage and disc space narrowing(123–125).

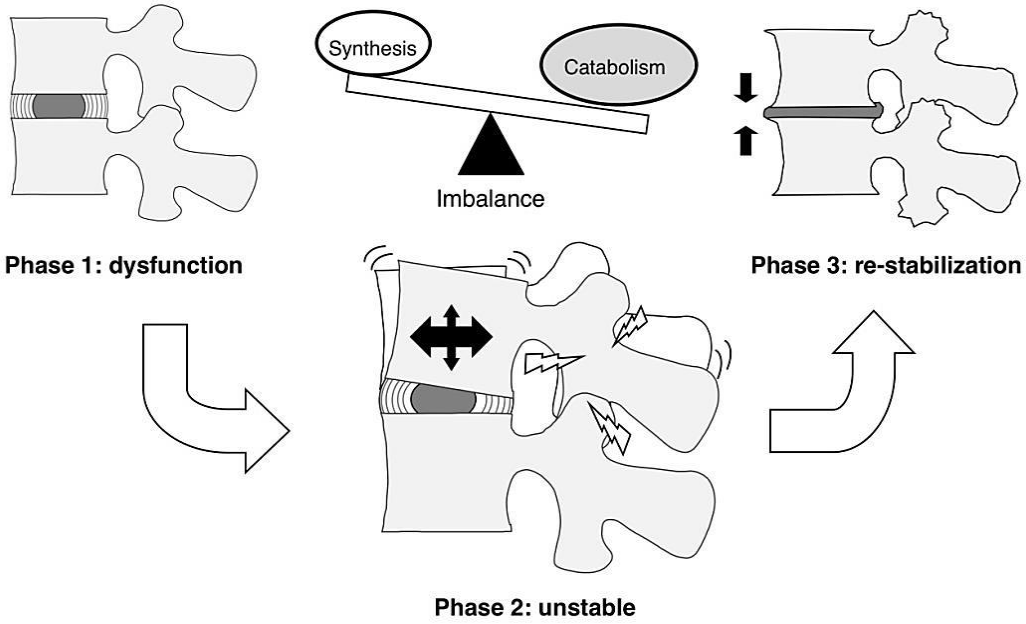


The disc ages through a sequence of stages as a result of biomechanical, biochemical and inflammatory factors, these stages are known as the degenerative cascade. The normal physiological microtrauma causes annular fissuring and tears which is the dysfunctional phase. Water content of the nucleus pulposus decreases and the nature of the proteoglycans change leading to reduction of hydrostatic pressure thereby decreased disc height and alteration in load distribution. This results in overload of the annulus and facet joints, the annulus not able to withstand the compression gets multiple tears and the disc bulges or herniates decreasing the disc height further, leading on to delamination which is the instability phase. Such bulges or herniations may impinge on the cord or a nerve root resulting in radiculopathy, radicular pain may also be due to the leakage of inflammatory cytokines through the annular tears.

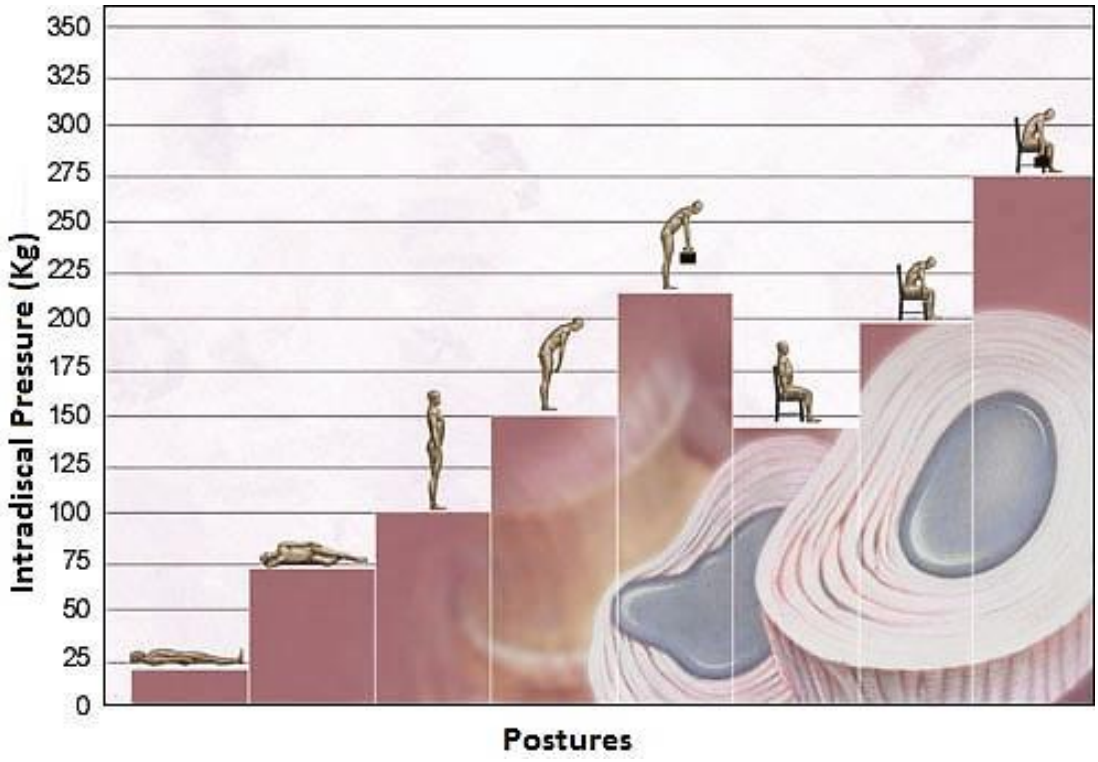


As a compensatory mechanism in response to the decreased disc height osteophytes are formed around the adjacent vertebra which is the phase of stabilization(126). The facet joints show features of arthritis due to the 40% increased loading of the neural arch(124). The nucleus herniates through the end plates and forms schmorl's node which may cause inflammation(123). These changes are irreversible in older age groups. Aging and various other factors together cause disc degeneration, but the mechanism of initiation of the process and its progress is still being evaluated(124,127). Male population tends to have more disc degeneration(128,129). Heredity has also been attributed in explaining the variability of natural disc degeneration in different population groups and many gene forms associated with disc degeneration have also been identified(130). The natural degeneration is higher at L4-L5 & L5S1, probably due to increased loading in that region (131,132).

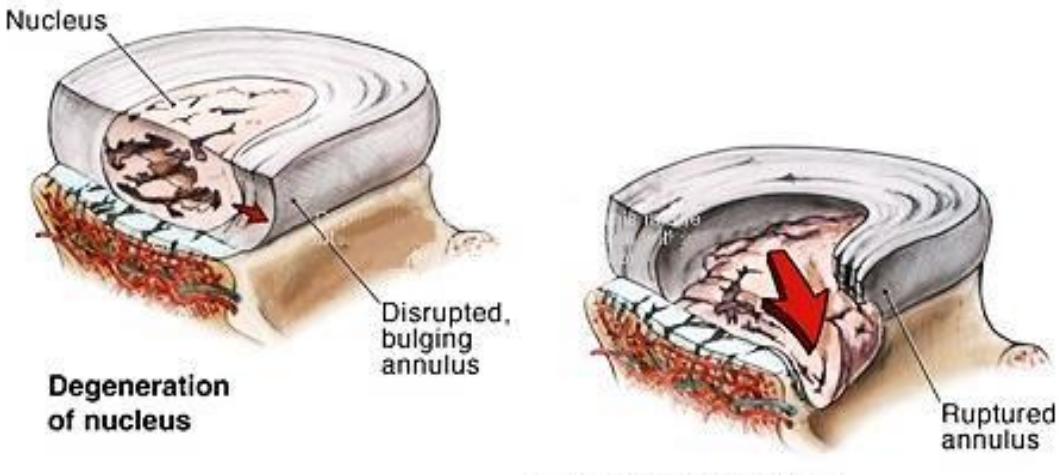
BIOMECHANICS OF DISC DEGENERATION:



The nucleus pulposus acts as a gelatinous mass, which decreases in volume when subjected to compressive forces. There is also an increase in the hydrostatic pressure, which causes bulging of the annulus. During the day the disc height decreases as the compressive load squeezes water out of the disc and the creep of the viscoelastic annulus collagen fibers, both these processes are reversible in a healthy disc with the unloading of the spine during bed rest(133,134). Longer the duration of spine loading greater is the annulus bulge and facet joint loading, there is alteration in the structure and function of the disc(135,136). Studies have shown that the posterior and posterolateral annulus have the highest risk for prolapse, especially in a normal or mildly degenerated disc. Moderate and severely degenerated discs have lower risk for prolapse(137).



Prolonged sitting leads to sustained axial loading altering the viscoelastic properties of the disc and the vertebra. There is increase in load across the disc at the resonant frequency of the spine 5 to 8 Hz range, which can occur during common postures in workplace. The nucleus pressure is 150% at the resonating frequency(138). Sitting with bending postures apply more pressure to the disc than standing and recumbent positions. There is variation in the intradiscal pressure with every posture,as illustrated in the above picture. Muscle dysfunction destabilizes the spine, decreases the facet joint loading and increases the loading of the disc and ligaments(139).



Disc space narrowing, increases the pressure between facets significantly(140). Damage to disc causes disproportionate loading of the facet joints (16). Discs at the adjacent level to a degenerated disc experience high tensile and shear forces during the end range of motion, they also noted that the facet joint motion at the degenerated and adjacent levels were altered(141). Disc degeneration leads to facet joint arthritis(142–145), but it may take more than 20 years to develop facet joint arthritis following the onset of disc degeneration and is therefore associated with grade IV and V Disc degeneration(146). Axial rotational motion is most affected with disc degeneration and the effects of disc degeneration on the motion were similar between genders, facet joint arthritis affected the segmental motion(147). The amount of disc degeneration differs with each patient and so do the treatment options, ranging from conservative treatment to surgical intervention aimed at relieving the pain, prevent progression of degeneration at the same level and the adjacent levels. Surgical treatment also ranges from simple discectomy, fusion to total disc arthroplasty(1).

BIOMECHANICS OF SPINAL INSTRUMENTATION:

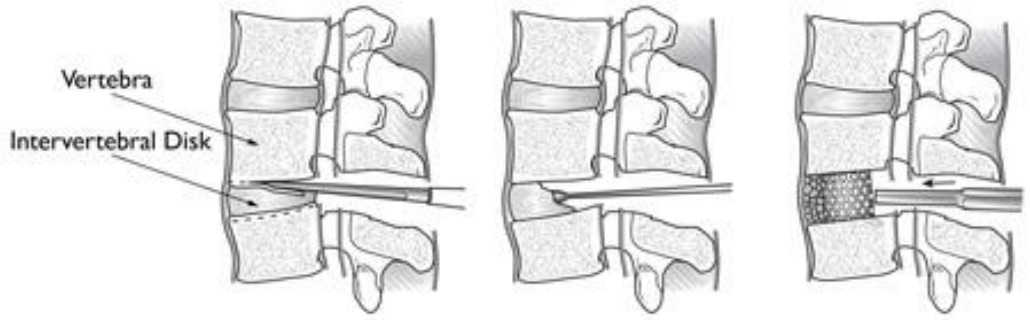
Implantation of spinal devices is to alter the abnormal biomechanics of spine caused by the degeneration to near normal biomechanics. The implants can be evaluated by comparing the stability of the implant to that of an intact spine. The effects of decompression and stabilization by these implants are tested using in-vitro studies and finite element based biomechanical studies using standard test protocols, thereby providing information regarding safety and effectiveness of the implants before clinical use(149–151).

Fusion causes movement limitation of the involved level and therefore reduces further degeneration and relieves pain. The main indications for fusion are prolonged back pain, recurrent disc prolapse, instability and failed conservative treatment(1). Spinal fusion surgery can be either with or without instrumentation and bone grafting. Pseudoarthrosis is occurs in cases of fusion without instrumentation. Cages filled with bone graft are used, such bone grafts in-between the vertebrae experience 80% load and occupy 90% of bony area with rich vascularity thereby enhancing fusion(152). Spinal instrumentation maybe in the form of pedicle screw system and rods, plates, clamps and wires. Pedicle screw system is effective in achieving high fusion rates(153). Jutte et al. reported a 0.9% of Implant failure, others reported rod fractures, screw cutting out(154–157). The success of fusion is to achieve arthrodesis in order to provide stability and relieve pain, the present day techniques achieve fusion in 95% of cases and pain is relieved

in only 70% of cases(158). The chief complication of fusion is adjacent segment degeneration. Some authors claim it to be part of the natural aging process while others argue it to be due the fusion (159).

BIOMECHANICS OF LUMBAR INTERBODY FUSION:

Lumbar interbody fusion was described by Capener in the 1930's, many techniques have been described later. The basic goal of interbody fusion is a mechanically stable construct that restores disc height, increases foraminal dimensions, coronal and sagittal balance(160). Surgical approach, implant choice and position are very important.



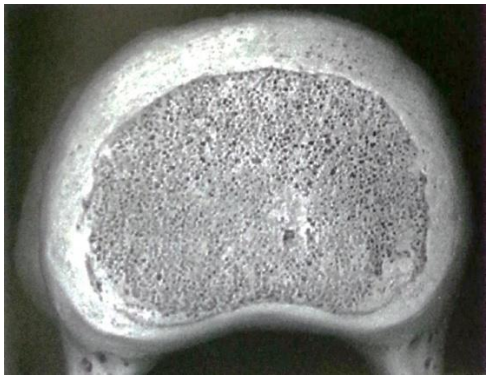
The lumbar spine when loaded behaves like a flexible and compressible column. The spine is made up of alternating rigid bony structures and flexible soft structures in the form of vertebral bodies and the intervertebral discs, anterior and posterior longitudinal ligaments, paraspinal muscles and posterior ligamentous complex(161).

A successful interbody fusion is well described by Wolff's law, according to which, adaptive remodeling of bone occurs on application of stress in order to resist the stress better(162). Initially discectomy is done following which the graft bed is prepared and then the interbody spacer and the bone graft are inserted in the load-bearing axis of the spine. In an ideal situation there is optimal distribution of load

shared between the implant and the bone graft. Stress shielding is defined as an implant induced reduction of load on the bone to an extent that stress reduction osteopenia or pseudoarthrosis occurs(163).When there is too much load on the implant, the bone graft does not get enough stress that is needed for healing; This causes delayed union or nonunion, secondary to stress shielding; ultimately leading to implant failure or subsidence causing loss of intervertebral height.

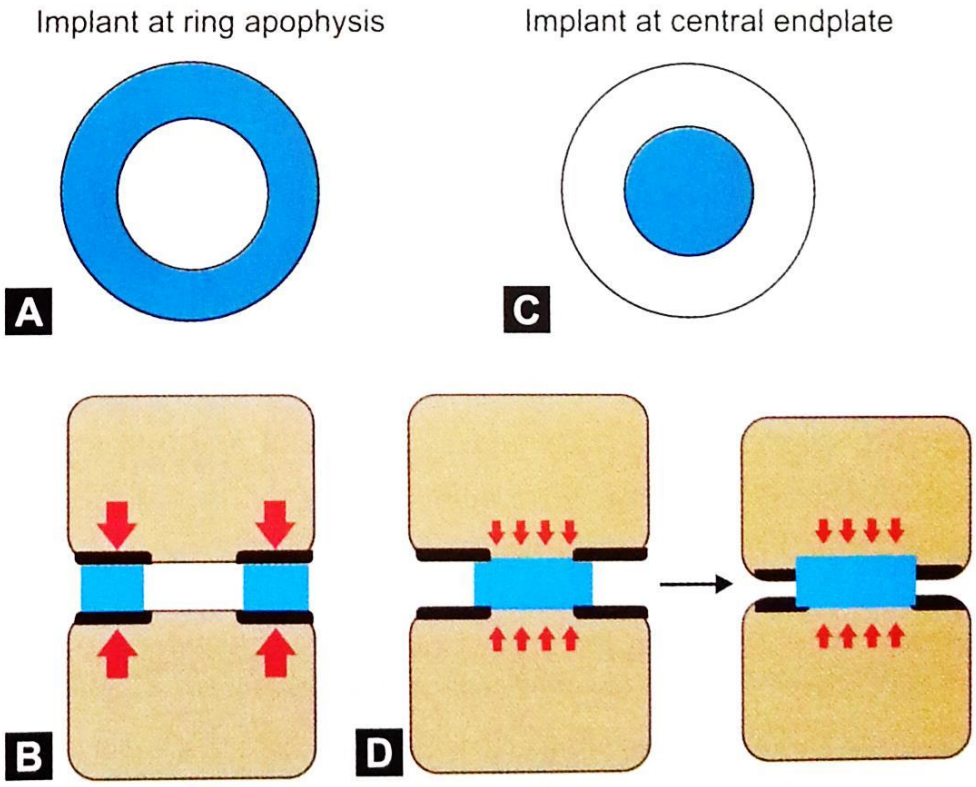
The implants are placed in the disc space to restore the disc height and also to provide mechanical support, and its purpose is to maintain alignment and stability till there is arthrodesis. The commonly used weight bearing spacers are autograft, allograft and synthetic cages.

The concept of distraction-compression for mechanical stability(164) is used here; the intervertebral space is distracted by the implant stretching the annulus into tension. Evans compared this to a flagpole; the interbody spacer being the flagpole bears the compressive load and the distracted and fixed annulus and posterior ligaments being the tensioned cables bear the tensile load(161).



Vertebral endplate showing the ring apophysis and the central cancellous bone

To avoid graft subsidence the implant should be placed along the endplates. The inferior endplate is stiffer and 40% stronger than its superior counterpart. The outer rim of the endplate which is called the ring apophysis is stronger than the central region. The cortex of the vertebral body is capable of bearing heavier loads than the central cancellous part. So when the forces are distributed along the ring apophysis the axial load bearing capacity is superior.

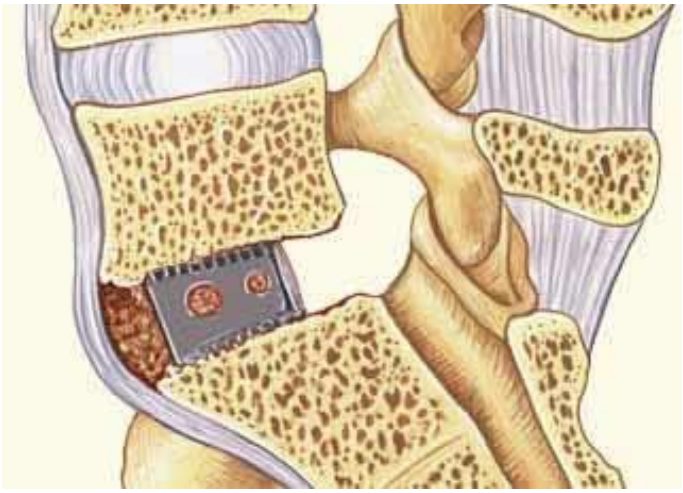


A- Cross sectional view of the intervertebral space with an implant placed peripherally
B- B- A sagittal view of the peripherally placed implant.
C- Cross sectional view of a centrally placed implant.
D- Sagittal view showing the subsidence due to prolonged stress-concentration.

The cartilaginous endplate and the outer cortex is removed before placing the fusion device(165). Clearing of the fusion bed helps in increasing the surface

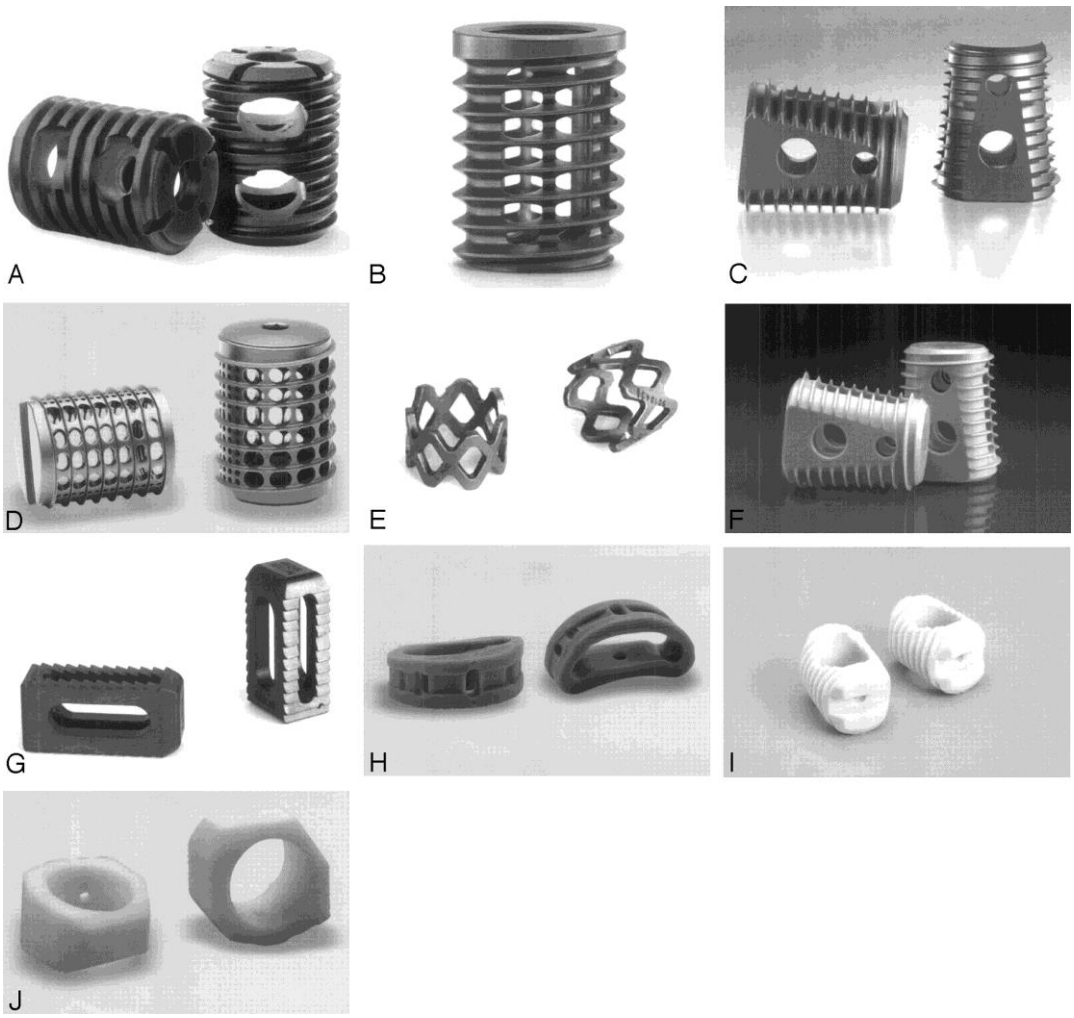
contact area and bony ingrowth into the implant. It is found that if the endplate is removed there is 50% decrease in its integrity(166,167). Increased movement in the bone implant interface hampers fusion, bone mineral density is found to be indirectly proportional to the bone implant interface motion. Using of cages significantly decreases the intervertebral movements in flexion and lateral bending. Adding pedicle screws, rods or plates improves the stabilization in flexion, extension, lateral bending and axial rotation(160,168–173).

Interbody cages:



The interbody spacer is the key for a successful fusion; they help in stabilization by restoring disc height, maintaining lordosis and directing load transmission through the anterior column(174). There are many choices of spacers for reconstruction of the anterior column. The geometry, size and materials used for grafting are all influential in the success of fusion. The commonly used graft materials are: autograft (iliac crest, fibular strut), allograft, titanium mesh cages,

polymeric cages (polyetheretherketone [PEEK]), rhBMP-2 and ceramics. Because of complication of bone harvesting and the availability, biocompatibility and proven efficiency of the synthetic material, the use of autograft as interbody spacer has deteriorated. Local bone graft or allografts are used by packing into the cages as bone grafts.



Cage designs are important in preventing subsidence and creating stability, there are many designs like threaded, cylindrical titanium mesh, rectangular and wedge-shaped cages. The wedge shaped cages are preferred since their geometry improves lumbar lordosis and restores sagittal balance, so they are preferred for avoiding flat-back deformity in PLIF.

The surface area of the endplate-graft interface is also important, pseudoarthrosis can occur from inadequate contact. The graft should cover atleast 30% of the endplate area for good weight bearing capacity without subsidence(175). Maximizing the contact area between the cage and the endplates and circumferential placement of bone graft around the cage results in near normal physiological stress distribution(176,177). Use of wider cage allows more efficient transfer of force, through better contact with the peripheral endplates(178). Larger implants reduce the peak contact pressures and increase the implant-endplate contact area(177).

The cage material may be stainless steel, titanium alloy, ceramic, carbon fiber or polymer (PEEK). The ideal graft should be biocompatible, modulus of elasticity similar to bone, strong, radiolucent and cost effective. PEEK has elastic modulus of 3.6GPa, which is closer to that of cortical bone (12GPa) and it is radiolucent(179). Titanium is biocompatible, strong, and resistant to corrosion, minimal radiographic distortion in comparison to stainless steel. The modulus of elasticity is 110GPa half that of stainless steel but ten times that of bone. Newer titanium alloys like beta-

titanium have increased fatigue strength and lower elastic modulus. Carbon fiber has similar modulus of elasticity as bone and is radiolucent, but it causes tissue reactivity. Carbon-fiber reinforced PEEK (CFRP) has high fatigue strength, high chemical stability, no metal ion release, radiolucency and biocompatibility and its modulus of elasticity is 13 GPa(180–184).

The surgical approach also interferes with the implant choice and positioning. There are various approaches like Anterior (ALIF), Posterior (PLIF), Transformational (TLIF) and extreme lateral (XLIF). In the posterior approaches (PLIF and TLIF) access to the disc space is more limited when compared to anterior approaches (ALIF and XLIF). ALIF allows placement of the cages with wide footprints over the ring apophysis, the cages are usually trapezoidal in shape allowing better correction of sagittal balance. In XLIF technique a long slender cage is used and is placed transversely across the intervertebral space. The ALL and PLL are spared, giving additional stability and aids in bone formation(185). In PLIF and TLIF techniques smaller cages are used, they are placed avoiding traction of the neural elements. The cages rest on the posterolateral apophyseal ring.

BIOLOGY OF SPINAL FUSION:

Biology of spinal fusion is a complex process that requires the perfect coordination of molecular, cellular and structural events. The fundamental requirements of a good spinal arthrodesis are blood supply, osteoinductive factors and osteogenic cells, osteoconductive scaffold and a good mechanical environment. Blood supply provides oxygen, nutrients, controls pH and helps in recruitment of cells. Osteogenic cells are in the decorticated local bone and in the bone graft, surrounding soft tissue are a source of osteoprogenitor cells and also fibroblastic cells that inhibit bone bridging. Osteoinductive growth factors are expressed throughout the healing(186). Good surface area of decorticated bone with exposure to bone marrow is important for fusion. The graft is an osteoconductive region where the cells from the marrow reach.

Local factors like soft tissue trauma, tumor, infection and scarring from previous surgeries are of great disadvantage. Host factors which can inhibit bone healing are malnutrition, nicotine, corticosteroid, NSAID use and chemotherapy. The osteogenic potential of a graft is based on the survival of live osteogenic precursor cells. Osteoconductive graft acts as a scaffold allowing vascular and cellular invasion and osteoblast differentiation, the graft resorbs and is replaced by new bone by creeping substitution. Osteoinduction is a process in which growth factors stimulate mesenchymal cells to form chondrogenic and osteogenic cells. The bone grafts should also be biocompatible and resistant to mechanical compression.

Three phases of spinal fusion are: Inflammatory, reparative and remodeling(187). The inflammatory phase occurs within the first few weeks, starting with hematoma formation followed by influx of inflammatory cells. A fibrovascular stroma is formed which later undergoes neovascularization. Osteochondroprogenitor cells are recruited by the cytokines which are released by the inflammatory cells. The reparative phase is characterized by Intramembranous bone formation over the transverse processes. In the remodeling phase there is maturation of the fusion mass through resorption and membranous bone formation along the stress lines, within 6 months it begins to stabilize(188).

The healing of spinal fusion also involves at the molecular level certain growth factors and cytokines like platelet derived growth factor (PDGF), tumor necrosis factor α and β(TNF-α and TNF-β), interleukins 1,6,10,12, Insulin-like growth factor and bone morphogenetic proteins.

ADJACENT SEGMENT DEGENERATION:

Definition:

Adjacent segment degeneration is the radiological changes of degeneration seen in the caudal or cephalic adjacent functional spinal unit following a single or multiple level spinal fusion surgery. The onset of new symptoms such as radiculopathy, myelopathy, discogenic pain or instability etc., corresponding with the radiographic changes is adjacent segment disease(189).

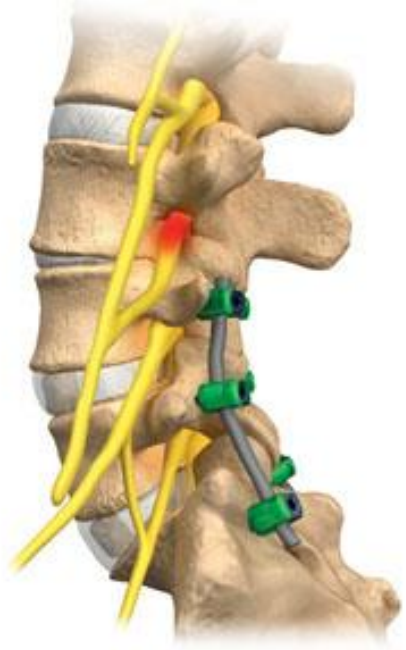


Illustration showing Adjacent Segment Degeneration in the Cephalic Segment

Etiology:

There has been a prolonged universal debate as to whether the adjacent segment degeneration is a continuation of the natural degenerative

process(190,191) or if it was directly related to the biomechanical changes caused by the surgical intervention itself(192,193). There have been numerous studies supporting both the ideas. The impact of adjacent segment degeneration on the clinical outcome seems significant(194) but Okuda et al observed that it is not(195). Some authors believe it is due to reduced motion caused by the fusion, while others believe it may be due to hypermobility, increased disc pressure, increased facet joint pressure and alteration in histological properties of ligaments at the adjacent segment(159,196–201). Biomechanical studies have proven that there is increase in the adjacent disc pressure and motion(202,203) and increase in the load and shear stress of the posterior column(204). The caudal adjacent disc experience increased loading with increasing length of instrumentation but the cephalic adjacent disc remains unaffected(197,205). Cunningham et al in their cadaveric study found that destabilization and instrumentation causes increase in proximal disc pressure up to 45%(206).

Incidence:

There is a big margin of difference among the reported incidence of adjacent segment degeneration. A systematic review and metaanalysis conducted by Xiao-Peng Xia et al revealed that the incidence of adjacent segment degeneration ranged from 4.8% to 92.2% and the incidence of adjacent segment disease ranged 0% to 30.3%(189).

Risk Factors:

- Patient Factors:

Patients over the age of 60 years at the time of index surgery are found to be at higher risk of developing adjacent segment disease (207–210). But Okuda et al(211) did not find any significant association with age. Nonsmokers are more likely to have better outcome. Comorbidities do not modify the effect of fusion(212). Female gender and high body mass index may be significant(213,214).No correlation was found with bone mineral density and adjacent segment degeneration(208).

- Radiological factors:

Presence of pre-operative disc degeneration, facet degeneration and sagittal imbalance puts the patient at a higher risk(207,210). Large pelvic incidence angle, small lumbar lordotic angle, variation from the normal C7 plumbline - middle axis and sacral inclination increased the incidence(215–218). Pre-existing horizontalization of the lamina is as a pathoanatomic risk factor(219) especially in the cephalic segment and coexistence of lamina horizontalization and facet tropism accelerates the degeneration(211). No significant correlation was found with the disc height, lumbar lordosis, scoliosis(195), dynamic Intervertebral space angulation, displacement of the cranial vertebral body (208) and laminar inclination(211).

- Surgical Factors:

Anatomy disruption adjacent to the surgical level is a potential cause for adjacent segment disease(220,221). Lower lumbar fusions, multilevel fusion, circumferential procedures, stopping a construct at L5, excessive disc height distraction and post-operative disc space narrowing increase the risk for adjacent segment degeneration(210,222–224). Maintenance of sagittal alignment of the spine influences the incidence of adjacent segment degeneration(222,225,226). Hilibrand et al observed that adjacent segment disease was less in multilevel fusions when compared to single level fusions(227). Decompressive laminectomy along with posterior fusion increases the risk for adjacent segment degeneration(228). A potentially modifiable risk factor is protection of facet joint during pedicle screw placement(193). Fusion with instrumentation itself is a risk factor but because of the high rate of pseudoarthrosis reported with fusion without instrumentation(229,230), it is inevitable.

AIMS & OBJECTIVES

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AIMS:

The aim of the study is to find out the incidence of Adjacent Segment degeneration and the prevalence of adjacent segment Disease among them in our population and relate it with the risk factors taken into consideration. The findings can be used for better patient advice, patient selection, take adequate precautions with regards to surgical techniques and post-operative protocols. The hypothesis is that the Adjacent segment degeneration is not aggravated due to PLIF and if the incidence of adjacent segment degeneration is similar in the discectomy group of patients then it will support the theory that it is part of the natural history of disc degeneration.

OBJECTIVES:

A. Determining Incidence of adjacent segment degeneration, its impact on the outcome after fusion and discectomy.

B. Compare the two groups to understand the natural history of degeneration and influence of instrumented fusion.

MATERIALS & METHODS

MATERIALS AND METHODS:

This is an Ambidirectional cohort study; we studied the patients who underwent single level fusion in the form of instrumented posterior lumbar interbody fusion between the years 2006 and 2010. They were followed-up in the outpatient department with a minimum of 2 year period post-operatively. Since the intervention was in the past, and occurrence of adjacent segment degeneration is later looking from the starting point of the study and since we took the PLIF group of patients in one arm and discectomy patients in the other arm this study is a Ambidirectional cohort study. The reported time for the occurrence of radiological adjacent segment degeneration was an average of 25 months (79, 80). The incidence of adjacent segment degeneration and its consequence; the adjacent segment disease were determined by comparing with their pre-operative status. Certain risk factors like patient age at the time of surgery, gender, co-morbidities, occupation, smoking habit, physiotherapy compliance etc., were considered. The findings were compared with a well-matched control group of patients who underwent single level discectomy in the same period and evaluated with the same parameters like VAS, JOA and ODI.

Inclusion Criteria:

i. All the patients who underwent single level fusion and those who underwent single level discectomy in the lumbar region were included.

ii. A minimum 2 year period of follow-up was the requirement.

Exclusion Criteria:

i. Preoperative adjacent disc degeneration of more than Pfirrmanns grade III, to minimize the effect of natural disc degeneration.

ii. Any form of surgical intervention in the same or adjacent segment either with discectomy or fusion surgery.

iii. Patients who have undergone revision discectomy or instrumentation after the primary surgery.

Tools:

Plain X-Rays – antero-posterior and lateral views, including stress views and magnetic resonance imaging of the lumbosacral spine were done post-operatively and compared with the pre-operative images.

Variables:

The primary diagnosis for which the surgery was done, age, gender, co-morbid status, body mass index, occupation were all derived from the hospital records. The disc degeneration, facet degeneration, fusion and implant failure were assessed

from the pre-operative and post-operative radiographic imaging in the form of lumbosacral plain x-rays and magnetic resonance imaging. Patients' compliance to the physiotherapy was checked during the follow-up.

Data Measurement:

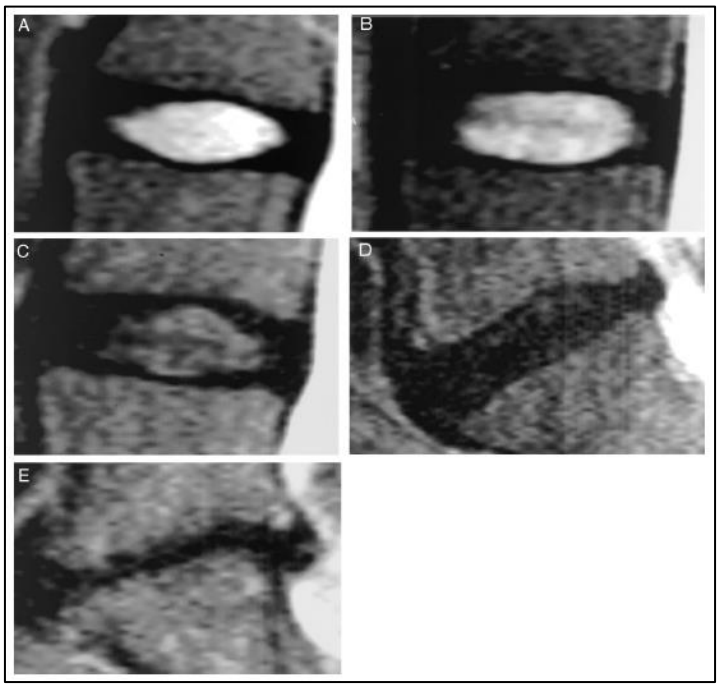
Radiological measurement for disc degeneration was with the MRI based grading as described by Pfirrmann et al.(231). Disc Height measured from plain radiographs(232). Fusion at the operated level was graded using Kyung Hoon Kim Modification of Brantigan-Steffee Criteria for fusion(233). Facet degeneration was graded as proposed by Fujiwara et al(234), using T2 weighted transverse cuts of the lumbar spine. Functional outcome was measured using Visual Analog Scale(VAS)(235–237), Oswestry Disability Index(ODI)(238), Japanese Orthopaedic Association Score(JOA)(239) and Hirabiyashi Recovery Rate(240).

Statistical Methods:

All statistical analysis was done using the SAS software version 9.2. For continuous data, the descriptive statistics such as mean, standard deviation, median, minimum and maximum were presented. For categorical data, the frequency and percentage were presented.

For categorical data, the bar chart is presented surgery wise with frequency. For continuous data, the difference was taken between post and pre-operative surgery wise. Histogram with plot was used to check the normality of data for the difference by surgery. For all data, univariate and bivariate analysis were performed.

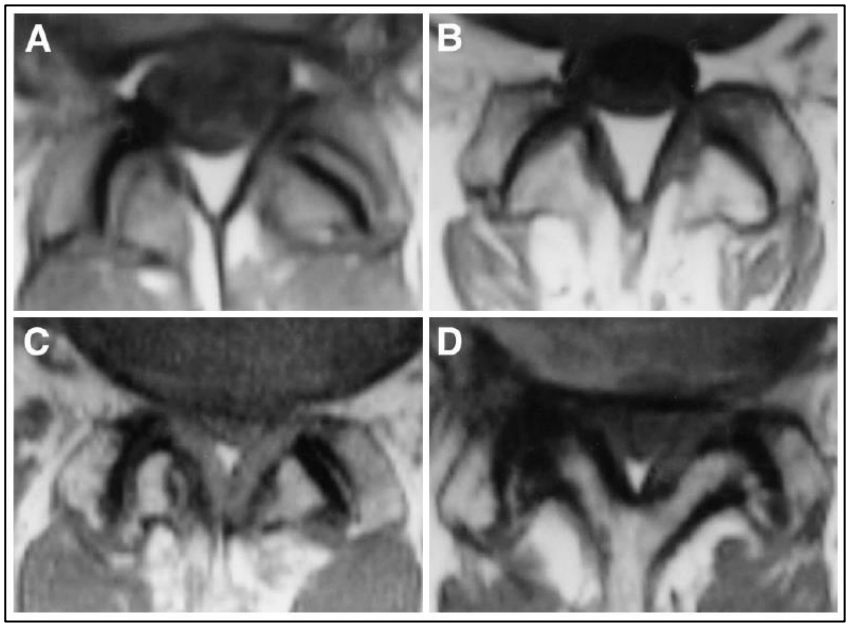
PFIRRMANNS GRADING FOR DISC DEGENERATION:



A=Grade-I, B= Grade-II, C=Grade-III, D=Grade-IV, E=Grade-V

Grade	Structure	Distinction of Nucleus and Anulus	Signal Intensity	Height of Intervertebral 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
Pfirrmanns Grading – T2-weighted sagittal images – MRI based				

FUJIWARA GRADING FOR FACET JOINT DEGENERATION:



Fujiwara grading - MRI based - T2-weighted TR images

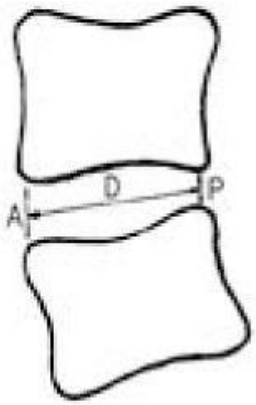
A- Grade 1:Normal, B- Grade 2:Joint space narrowing or mild osteophytes, C- Grade 3: sclerosis or moderate osteophytes, D- Grade 4: Marked

KYUNG HOON KIM MODIFICATION OF BRANTIGAN-STEFFEE CRITERIA FOR FUSION:

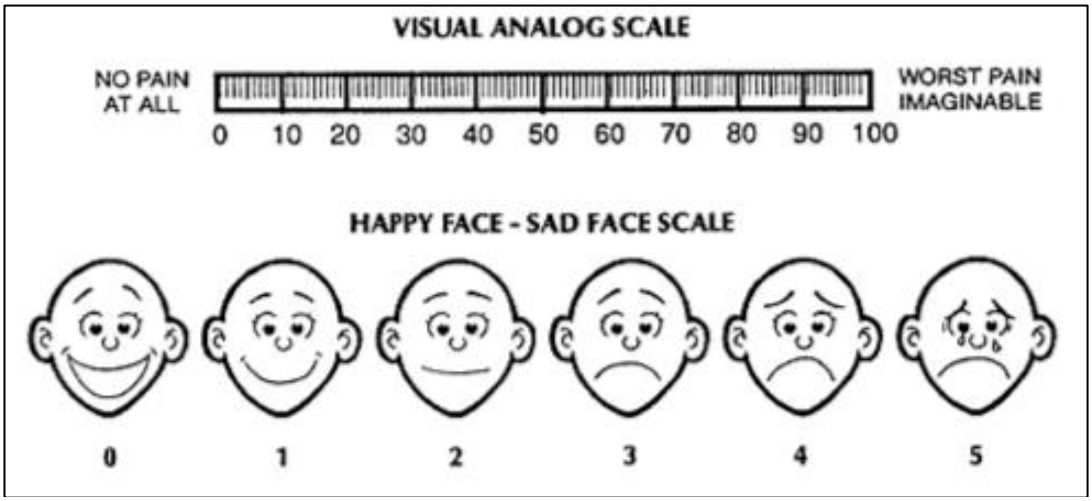
i. The bone fusion area is more dense and more mature than originally achieved during surgery.
ii. No interspace between the cage and the vertebral body
iii. Mature bony trabeculae bridging in fusion area
iv. And no traction spur

If one of the three criteria was not met it is non-fusion state.

DISC HEIGHT MEASUREMENT:



Disc space height = A+P/D



MODIFIED JOA BACK INDEX SCORE					
PARAMETERS	SCORES	PRE-OP	POST-OP	6 MTS	FINAL
BACK PAIN					
None	3				
Occasional mild Pain	2				
Frequent mild/ Occasional severe Pain	1				
Frequent Severe Pain/ Continuous Pain	0				
LEG PAIN					
None	3				
Occasional mild Pain	2				
Frequent mild/ Occasional severe Pain	1				
Frequent Severe Pain/ Continuous Pain	0				
GAIT					
Normal	3				
Able to walk > 500meters but causes pain/ tingling/ weakness	2				
Unable to walk > 500meters due to pain/ tingling/ weakness	1				
Unable to walk > 100meters due to pain/ tingling/ weakness	0				
SLR(INCLUDES TIGHT HAMSTRINGS)					
>70	2				
30-70	1				
<30	0				
SENSORY DISTURBANCES					
Normal	2				
Mild(Not subjective)	1				
Marked	0				
MOTOR DISTURBANCES					
Normal	2				
Mild(4-5)	1				
Marked(0-3)	0				
TURNING OVER WHILE LYING					
No restriction	2				
Moderate restriction	1				
Severe restriction	0				
SITTING > 1 HOUR					
No restriction	2				
Moderate restriction	1				
Severe restriction	0				
STANDING					
No restriction	2				
Moderate restriction	1				
Severe restriction	0				
WALKING					
No restriction	2				
Moderate restriction	1				
Severe restriction	0				
WASHING					
No restriction	2				
Moderate restriction	1				
Severe restriction	0				
LEANING FORWARD					
No restriction	2				
Moderate restriction	1				
Severe restriction	0				
LIFTING OR HOLDING HEAVY WEIGHT					
No restriction	2				
Moderate restriction	1				
Severe restriction	0				
URINARY BLADDER FUNCTION					
Normal	0				
Mild dysuria	-3				
Severe dysuria	-6				
TOTAL:	29				

HIRABIYASHI RECOVERY RATE:

$$\text{Hirabayashi recovery rate} = \frac{(\text{Post-operative JOA score} - \text{Pre-operative JOA score})}{(\text{Full score} - \text{Pre-operative JOA score})} \times 100\%$$

The Revised Oswestry Disability Index (for low back pain/dysfunction)

Patient name: _____ File #_____ Date: _____

SECTION 1-PAIN INTENSITY

- ☐ ☐ The pain comes and goes and is very mild.
- ☐ ☐ The pain is mild and does not vary much.
- ☐ ☐ The pain comes and goes and is moderate.
- ☐ ☐ The pain is moderate and does not vary much.
- ☐ ☐ The pain comes and goes and is very severe.
- ☐ ☐ The pain is severe and does not vary much.

SECTION 2-PERSONAL CARE

- ☐ ☐ I would not have to change my way of washing or dressing in order to avoid pain.
- ☐ ☐ I do not normally change my way of washing or dressing even though it causes some pain.
- ☐ ☐ Washing and dressing increases the pain, but I manage not to change my way of doing it.
- ☐ ☐ Washing and dressing increases the pain and I find it necessary to change my way of doing it.
- ☐ ☐ Because of the pain, I am unable to do some washing and dressing without help.
- ☐ ☐ Because of the pain, I am unable to do any washing and dressing without help.

SECTION 3-LIFTING

- ☐ ☐ I can lift heavy weights without extra pain.
- ☐ ☐ I can lift heavy weights, but it causes extra pain.
- ☐ ☐ Pain prevents me from lifting heavy weights off the floor, but I manage if they are conveniently positioned (e.g., on a table).
- ☐ ☐ Pain prevents me from lifting heavy weights off the floor.
- ☐ ☐ Pain prevents me from lifting heavy weights, but I can manage light to medium weights if they are conveniently positioned.
- ☐ ☐ I can only lift very light weights at the most.

SECTION 4-WALKING

- ☐ ☐ I have no pain on walking.
- ☐ ☐ I have some pain on walking, but it does not increase with distance.
- ☐ ☐ I cannot walk more than one mile without increasing pain.
- ☐ ☐ I cannot walk more than 1/2 mile without increasing pain.
- ☐ ☐ I cannot walk more than 1/4 mile without increasing pain.
- ☐ ☐ I cannot walk at all without increasing pain.

SECTION 5-SITTING

- ☐ ☐ I can sit in any chair as long as I like.
- ☐ ☐ I can only sit in my favorite chair as long as I like.
- ☐ ☐ Pain prevents me from sitting more than one hour.
- ☐ ☐ Pain prevents me from sitting more than 1/2 hour.
- ☐ ☐ Pain prevents me from sitting more 10 minutes.
- ☐ ☐ I avoid sitting because it increases pain right away.

SECTION 6-STANDING

- ☐ ☐ I can stand as long as I want without pain.
- ☐ ☐ I have some pain on standing, but it does not increase with time.
- ☐ ☐ I cannot stand for longer than one hour without increasing pain.
- ☐ ☐ I cannot stand for longer than 1/2 hour without increasing pain.
- ☐ ☐ I cannot stand for longer than 10 minutes without increasing pain.
- ☐ ☐ I avoid standing because it increases the pain right away.

SECTION 7-SLEEPING

- ☐ ☐ I get no pain in bed.
- ☐ ☐ I get pain in bed, but it does not prevent me from sleeping well.
- ☐ ☐ Because of pain, my normal night's sleep is reduced by less than 1/4.
- ☐ ☐ Because of pain, my normal night's sleep is reduced by less than 1/2.
- ☐ ☐ Because of pain, my normal night's sleep is reduced by less than 3/4.
- ☐ ☐ Pain prevents me from sleeping at all.

SECTION 8-SOCIAL LIFE

- ☐ ☐ My social life is normal and gives me no pain.
- ☐ ☐ My social life is normal, but increases the degree of pain.
- ☐ ☐ Pain has no significant effect on my social life apart from limiting my more energetic interests, e.g., dancing, etc.
- ☐ ☐ Pain has restricted my social life and I do not go out very often.
- ☐ ☐ Pain has restricted my social life to my home.
- ☐ ☐ I have hardly any social life because of the pain.

SECTION 9-TRAVELLING

- ☐ ☐ I get no pain while travelling.
- ☐ ☐ I get some pain while travelling, but none of my usual forms of travel makes it any worse.
- ☐ ☐ I get extra pain while travelling, but it does not compel me to seek alternative forms of travel.
- ☐ ☐ I get extra pain while travelling, which compels me to seek alternative forms of travel.
- ☐ ☐ Pain restricts all forms of travel.
- ☐ ☐ Pain prevents all forms of travel except that done lying down.

SECTION 10-CHANGING DEGREE OF PAIN

- ☐ ☐ My pain is rapidly getting better.
- ☐ ☐ My pain fluctuates, but is definitively getting better.
- ☐ ☐ My pain seems to be getting better, but improvement is slow at present.
- ☐ ☐ My pain is neither getting better nor worse.
- ☐ ☐ My pain is gradually worsening.
- ☐ ☐ My pain is rapidly worsening.

RESULTS

RESULTS:

From the year 2006 to 2010, a total of 305 single level posterior instrumented fusion (IPLIF) surgeries and 1161 single level discectomies were done. Among whom 129 single level discectomy patients and 68 single level IPLIF patients had come for follow-up.37 single level IPLIF and 59 single level discectomy patients who full filled the inclusion criteria were seen between April 2013 and September 2014 and analyzed. Among them36 were females (13-single level discectomy and 23-single level IPLIF) and 60 were males (46-single level discectomy and 14-single level IPLIF).

The average age among the discectomy group was 57(21-72) and the IPLIF group was 65(30-70). As far as comorbid status is concerned; 7 patients had diabetes mellitus, 9 had hypertension and 18 had other comorbid conditions. Occupation wise there were 25 heavy workers, 43 moderate workers and 19 sedentary workers, the occupation status of 9 patients were unknown. The moderate work group was found to be more in both the discectomy and IPLIF group of patients. Physiotherapy compliance was found to be poor as only 15% of the patients were doing regular physiotherapy. Smokers were found to be more in the IPLIF group. The average BMI in the group was 26.5. The average follow-up period among the discectomy patients was 70(24-92) months and among the IPLIF patients it was 75(28-94) months.

In the discectomy group of patients all the 59 patients had disc prolapsed of which 1(2%) had cauda equina syndrome.

Of the 37 patients who underwent single level IPLIF 33(89%) had spondylolisthesis, 4(11%) had infective etiology. Among the 33 spondylolisthesis 18(49%) were degenerative, 8(22%) were isthmic and 7(19%) dysplastic. Of the 33 spondylolisthesis 23(59%) were grade I, 8(22%) were grade II, 1(3%) was grade III and 1(3%) was grade IV. Infective pathology was seen in 4 patients out of which 1 was tuberculosis and the rest pyogenic.

Looking into the level of surgery; at the L3-4 level there were 7(12%) discectomies and 2(5%) IPLIFs, L4-5 level 31(53%) discectomies and 26(70%) IPLIFs, L5-S1 level 21(36%) discectomies and 9(24%) IPLIFs.

According to the Pfirrmanns grading system the incidence of disc degeneration was noted in the adjacent segments. Among the discectomy group the cephalic segment was degenerated in 35(59%) patients and the caudal segment was degenerated in 16(27%) patients by atleast 1 grade. There were 34(58%) patients with progress of degeneration by atleast 1 grade and 8(14%) patients with progression of degeneration by 2 grades.

There were 10(17%) patients who progressed from grade I to grade II, 7(12%) patients progressed from grade II to grade III, 17(29%) patients progressed from grade III to grade IV, 3(5%) patients progressed from grade I to grade 3 and 5(8%) patients progressed from grade II to grade IV in the patients who had atleast 1 level degeneration.

There were 42(71%) patients who had atleast one level disc (either cephalic or caudal level) degeneration.

Likewise in the IPLIF group the cephalic segment showed degeneration in 23(62%) patients and the caudal segment showed degeneration in 13(35%) patients by atleast 1 grade. There were 19(51%) patients with degeneration by 1 grade, and 7(19%) patients with degeneration by 2 grades. There were 5(14%) patients who progressed from grade I to grade II, 8(22%) patients progressed from grade II to grade III, 7(18%) patients progressed from grade III to grade IV, 5(14%) patients progressed from grade I to grade III and 2(5%) patients progressed from grade II to grade IV.

There were 26(70%) patients who had atleast one level disc (either cephalic or caudal level) degeneration.

According to the Fujiwara grading system the incidence of facet joint degeneration in the adjacent segment for discectomy patients were noted. The cephalic segment left facet joint was degenerated in 18(31%), cephalic right facet joint degenerated in 21(36%) and the caudal segment left facet joint showed 14(24%) and the caudal right facet joint was degenerated in 17(29%). Among them 24(41%) had either left or right cephalic facet joint degenerated and 20(33%) of them had either left or right caudal facet joint degenerated. There were 40(68%) patients with at least 1 facet joint degeneration by atleast 1 grade and 2(5%) patients with progression of degeneration by 2 grades. There were 15(25%) patients

who progressed from grade I to grade II, 24(41%) patients progressed from grade II to grade III, 1(2%) patient progressed from grade III to grade IV, 1(2%) patient progressed from grade I to grade 3 and 1(2%) patient progressed from grade II to grade IV.

There were 42(71%) patients who had degeneration of atleast 1 facet joint by atleast 1 grade.

According to the Fujiwara grading system the incidence of facet joint degeneration in the adjacent segment for single level IPLIF patients were noted. The cephalic segment left facet joint was degenerated in 15(41%), cephalic right facet joint was degenerated in 16(43%) and the caudal segment left facet joint was degenerated in 12(32%) and the caudal right was degenerated in 8(22%). Among them 19(51%) had either left or right cephalic facet joint degenerated and 14(38%) of them had either left or right caudal facet joint degeneration. There were 23(64%) patients with atleast 1 facet joint degeneration by atleast 1 grade and 6(16%) patients with progression of degeneration by 2 grades. There were 3(8%) patients who progressed from grade I to grade II, 9(24%) patients progressed from grade II to grade III, 10(27%) patients progressed from grade III to grade IV, 2(5%) patients progressed from grade I to grade III and 4(11%) patients progressed from grade II to grade IV.

There were 29(78%) patients with atleast 1 facet joint degeneration by atleast 1 grade

Discectomy patients were younger with a mean age of 40 years while the IPLIF patients mean age was 48. The male female ratio was reversed in both the groups i.e., more number of males underwent discectomy while more number of females underwent IPLIF surgeries respectively.

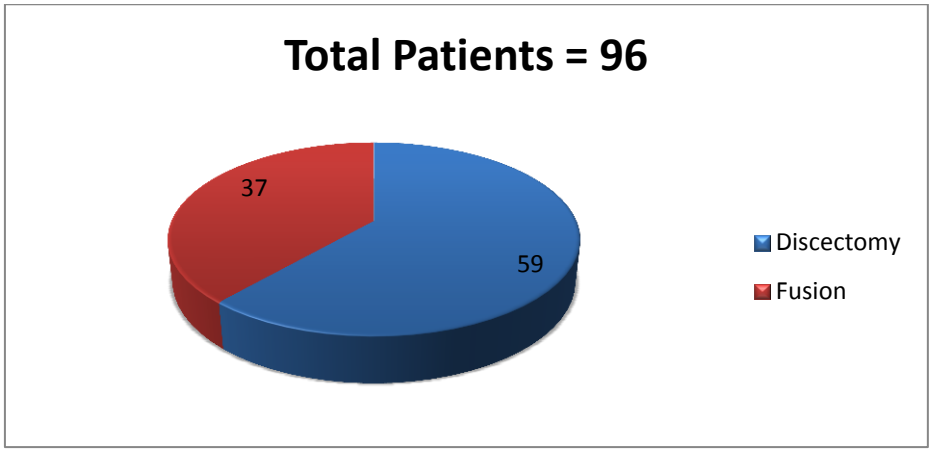
As per the Kyung Hoon Kim modification of brantigan-steffee criteria for fusion, to confirm the existence of fusion, all the IPLIF patients met the three criteria, i.e., they were all fused. There were no implant failures.

All patients showed improvement in the Visual Analog scale and JOA scores, only two patients showed poor results in their ODI and JOA scores, 1 was from the discectomy group who had L4-5 disc prolapse and the other from the IPLIF group who had Grade 2 isthmic spondylolisthesis, both were 4 years post-op, there were no other significant correlation between the confounding factors.

The overall incidence of adjacent segment degeneration, which includes disc and facet joint were evaluated and found to be (37) 71% among the discectomy patients and 27(74%) among the IPLIF group. Only one patient in each of these groups was symptomatic so the incidence of adjacent segment disease was 1.6% in the discectomy group and 2.7% among the IPLIF group of patients. The incidence of adjacent segment degeneration in the total 96 patients was (69)72% and that of adjacent segment disease was 2%.

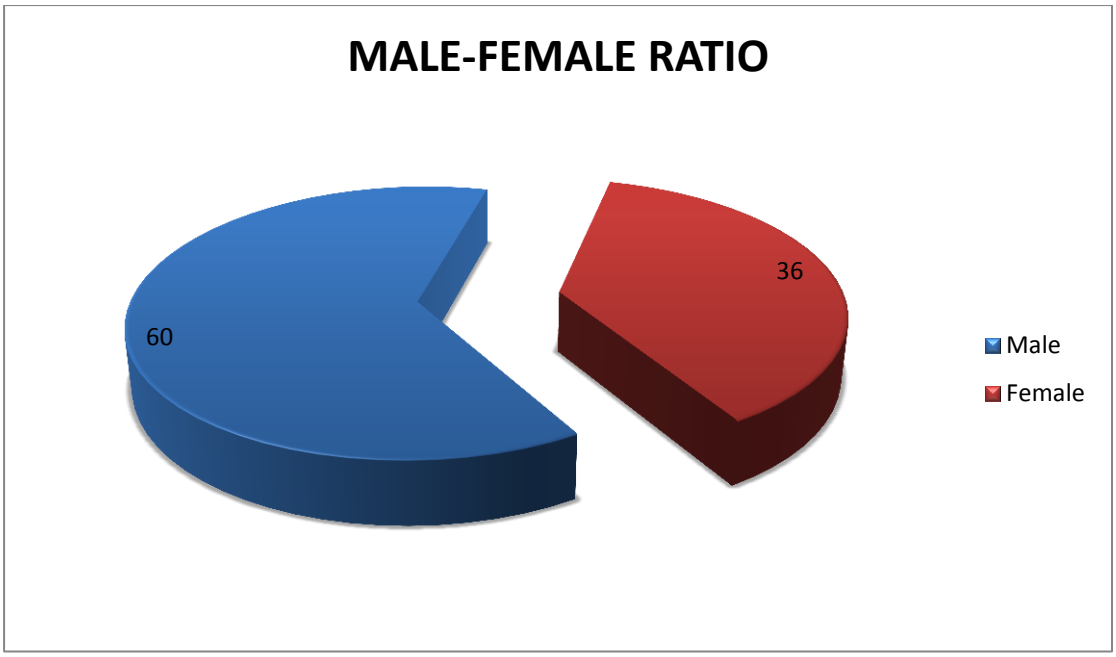
DATA ANALYSIS

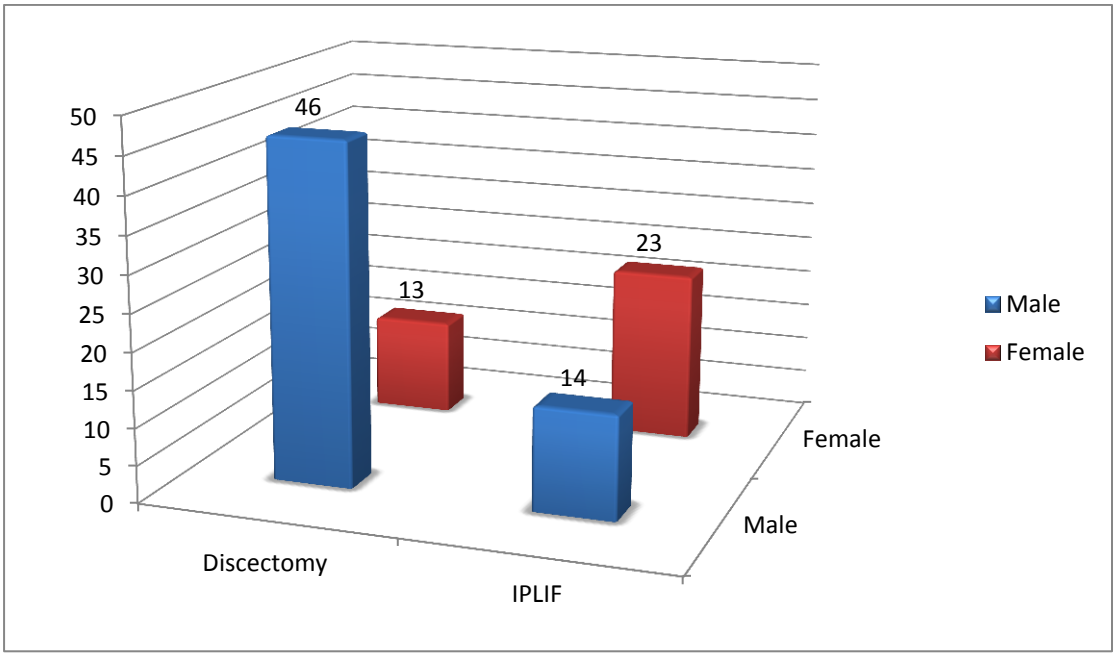
DATA ANALYSIS:

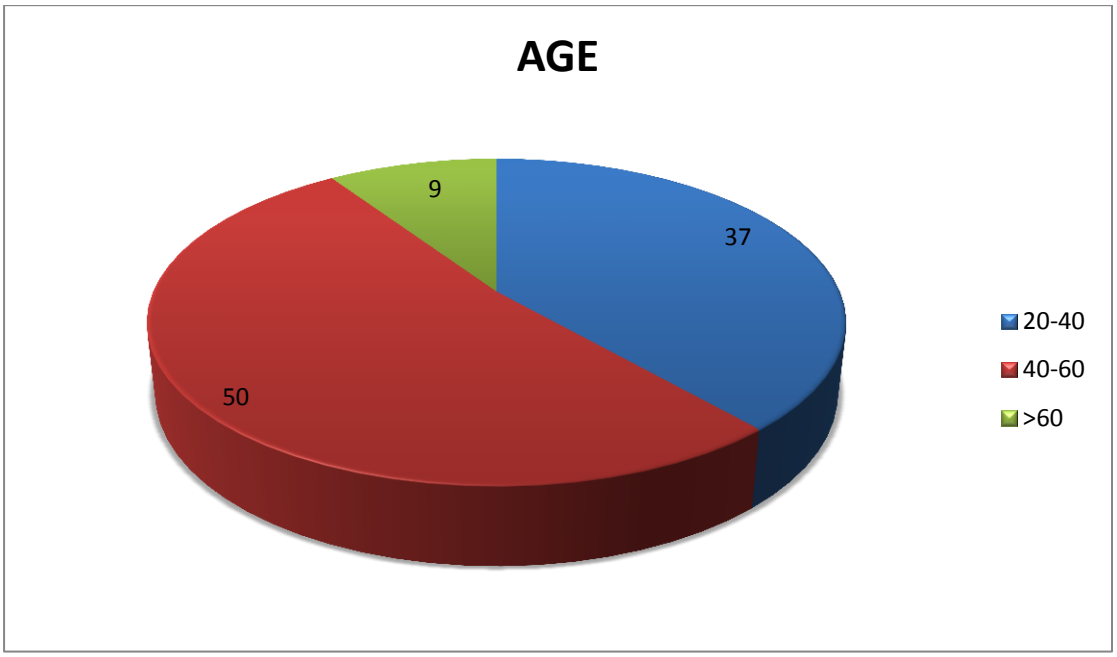


Statistic	DF	Value	Prob
Chi-Square	1	17.3164	<.0001
Likelihood Ratio Chi-Square	1	18.7683	<.0001
Continuity Adj. Chi-Square	1	14.8268	0.0001
Mantel-Haenszel Chi-Square	1	16.9400	<.0001
Phi Coefficient		-0.6136	
Contingency Coefficient		0.5230	
Cramer's V		-0.6136	

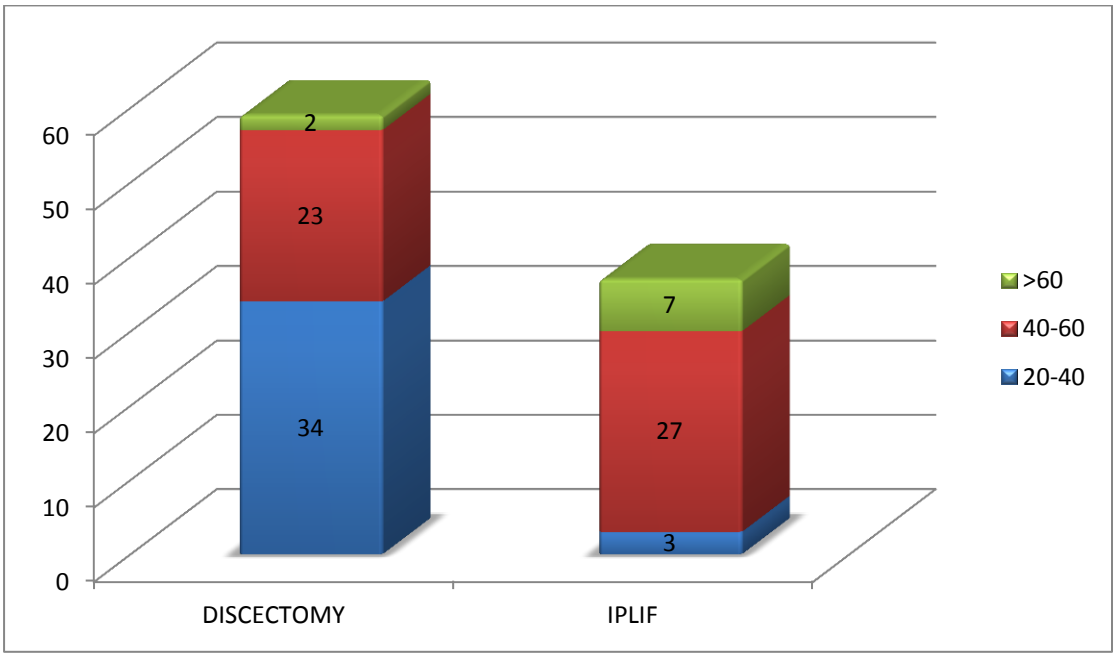
Fisher's Exact Test	
Cell (1,1) Frequency (F)	2
Left-sided Pr<= F	3.657E-05
Right-sided Pr>= F	1.0000
Table Probability (P)	3.518E-05
Two-sided Pr<= P	3.863E-05


MALE-FEMALE RATIO
60
36
Male
Female

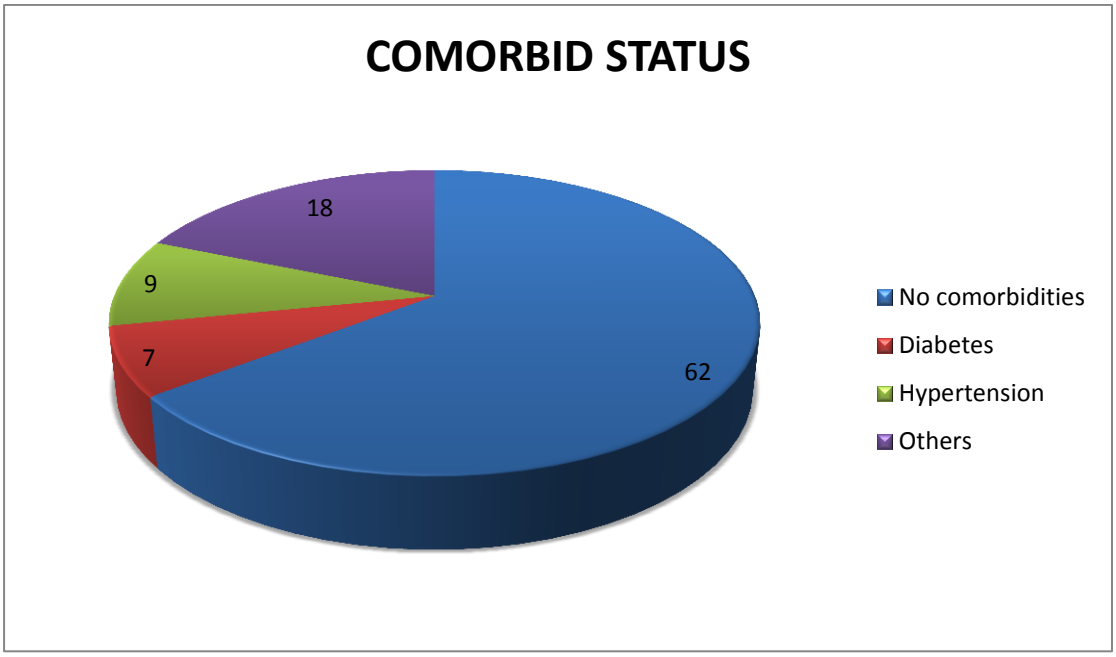

50
45
40
35
30
25
20
15
10
5
0
46
13
14
23
Discectomy
IPLIF
Female
Male
Male
Female

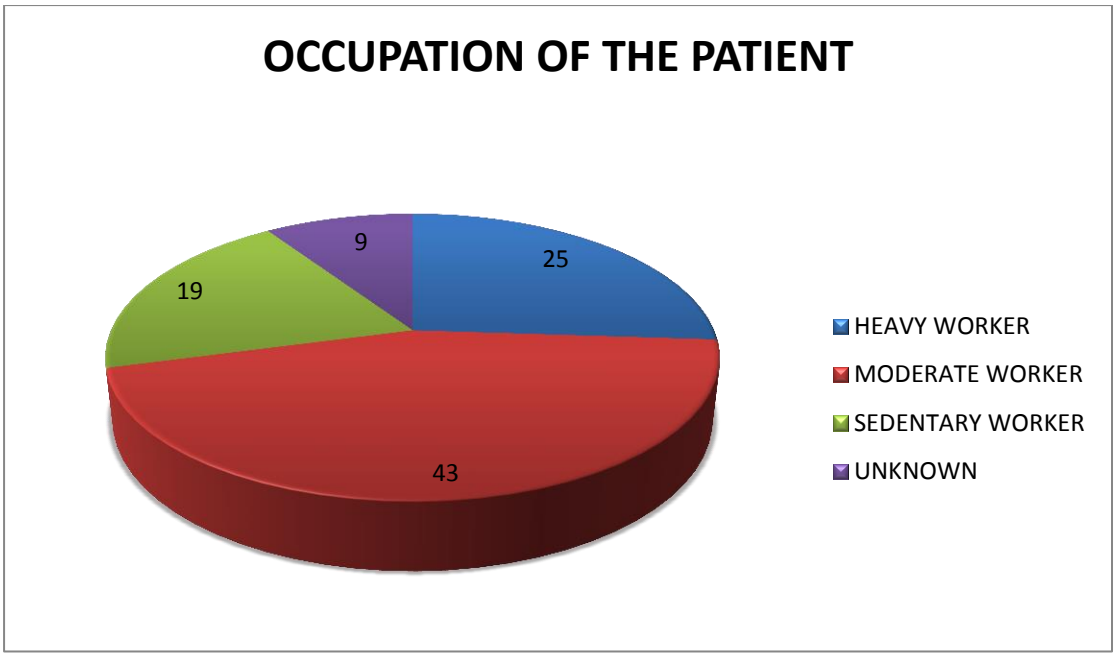


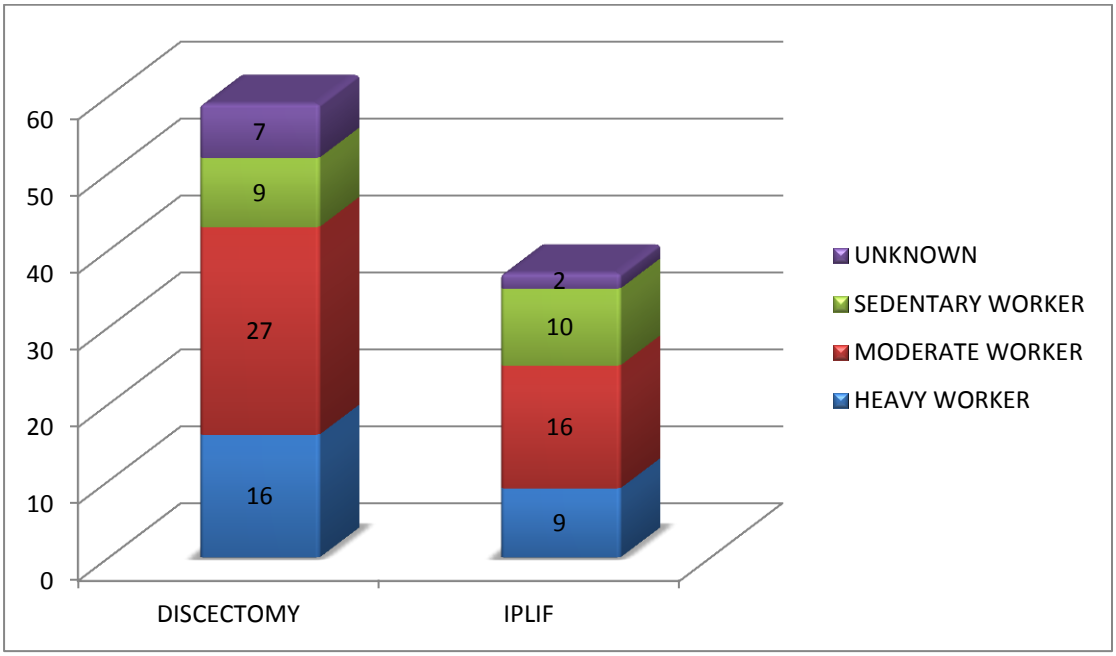
AGE DISTRIBUTION IN THE TOAL POPULATION

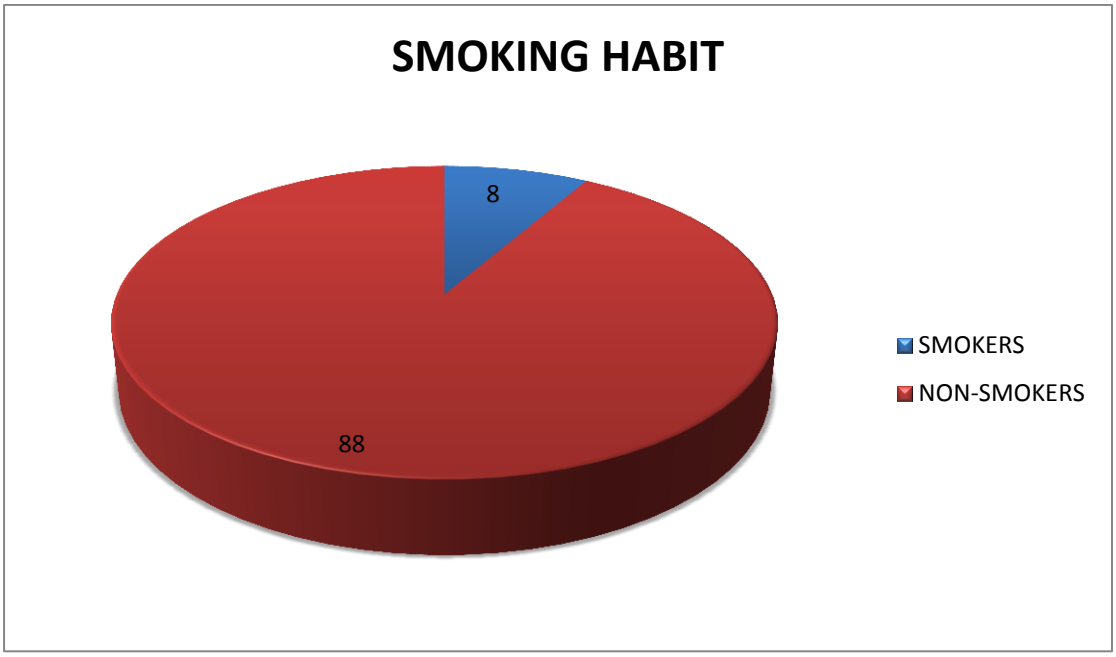


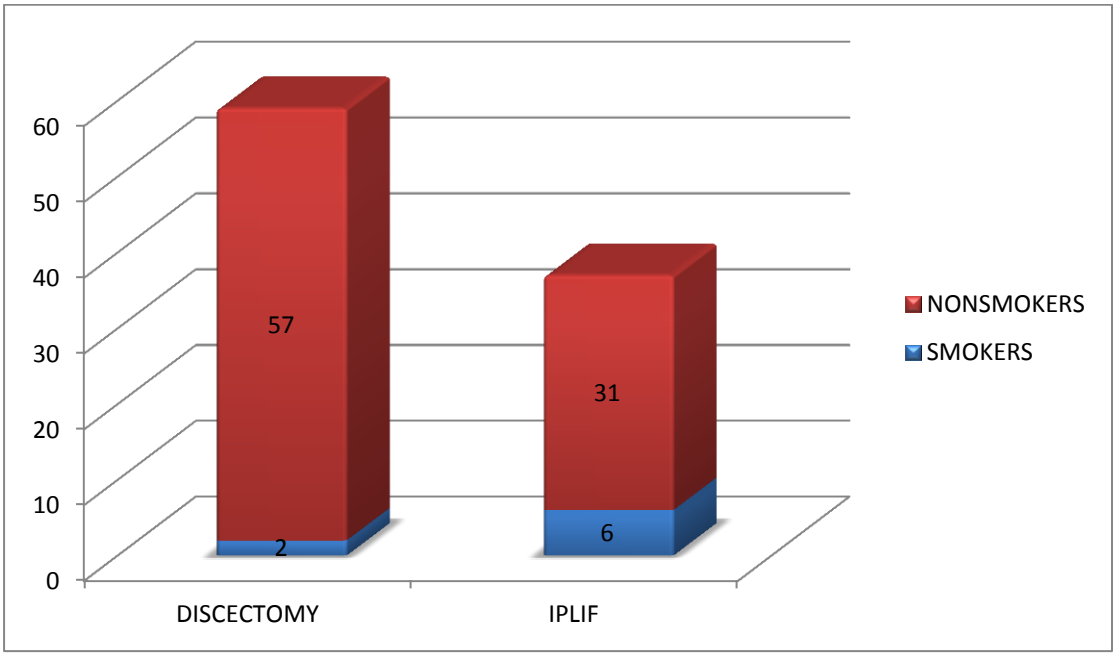
AGE DISTRIBUTION IN BOTH THE ARMS

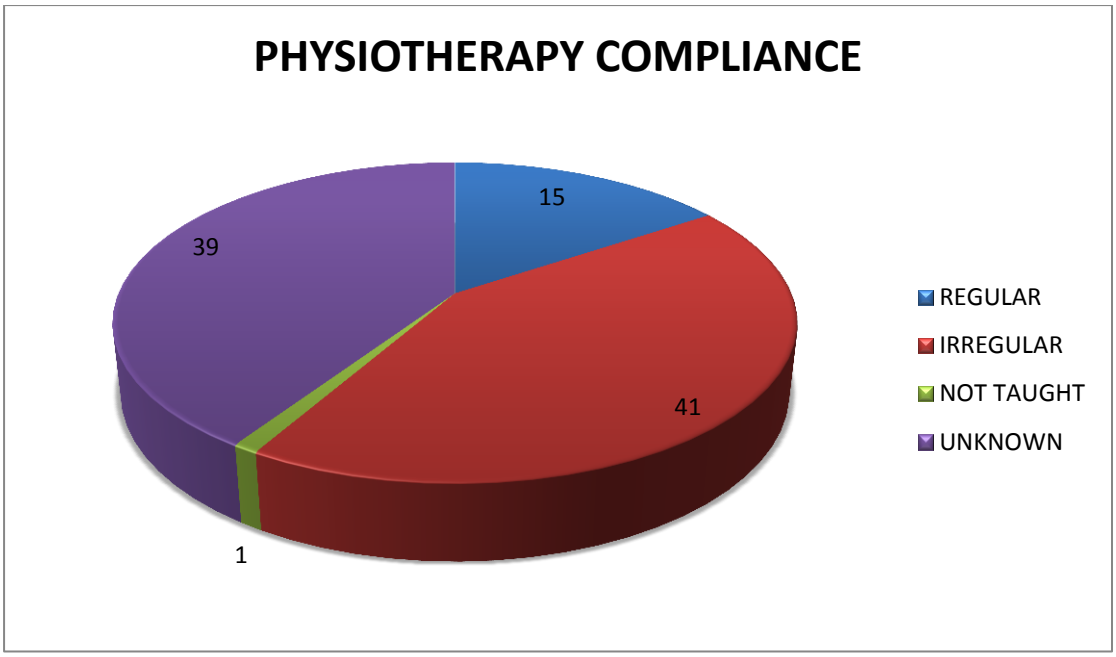

COMORBID STATUS
18
9
7
62
No comorbidities
Diabetes
Hypertension
Others

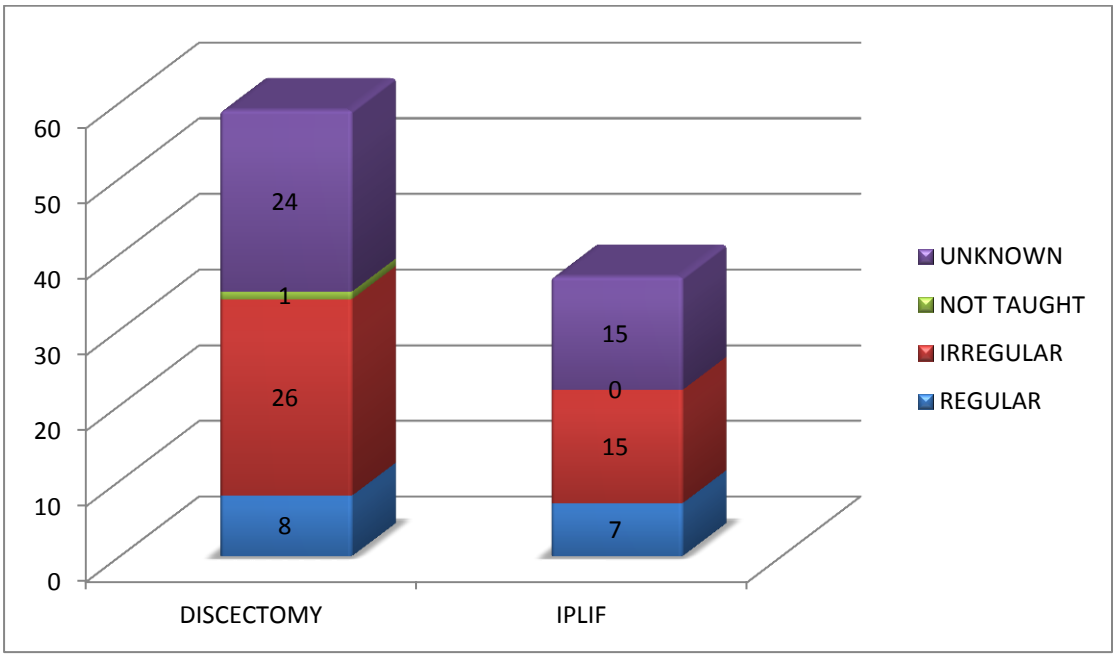

OCCUPATION OF THE PATIENT
9
25
19
43
HEAVY WORKER
MODERATE WORKER
SEDENTARY WORKER
UNKNOWN

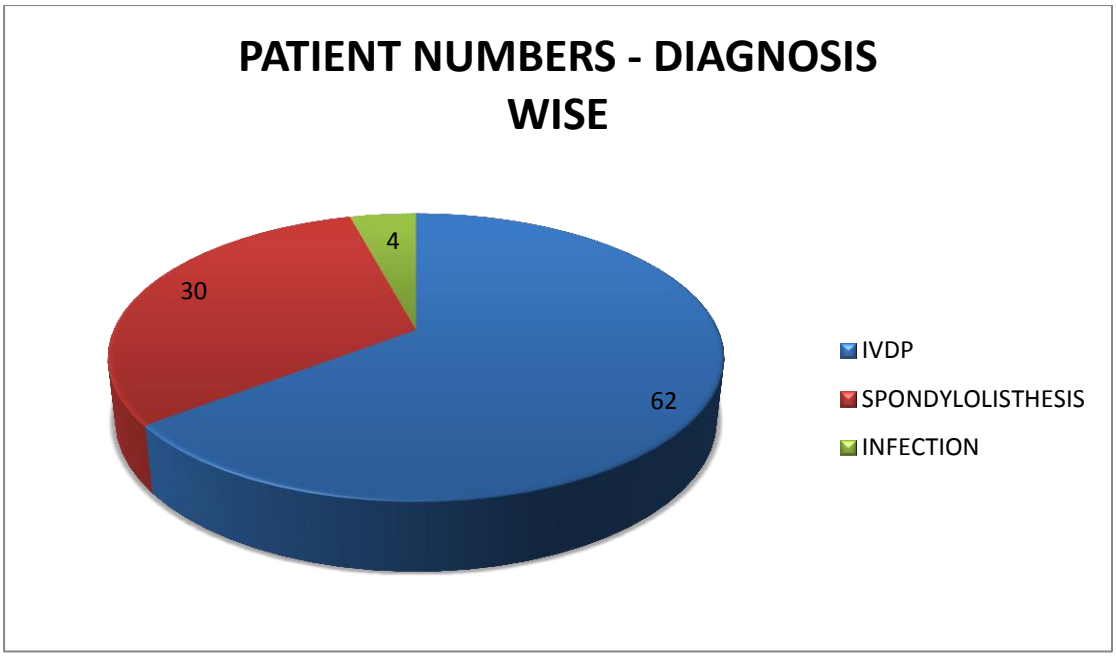

60
50
40
30
20
10
0
7
9
27
16
2
10
16
9
DISCECTOMY
IPLIF
UNKNOWN
SEDENTARY WORKER
MODERATE WORKER
HEAVY WORKER

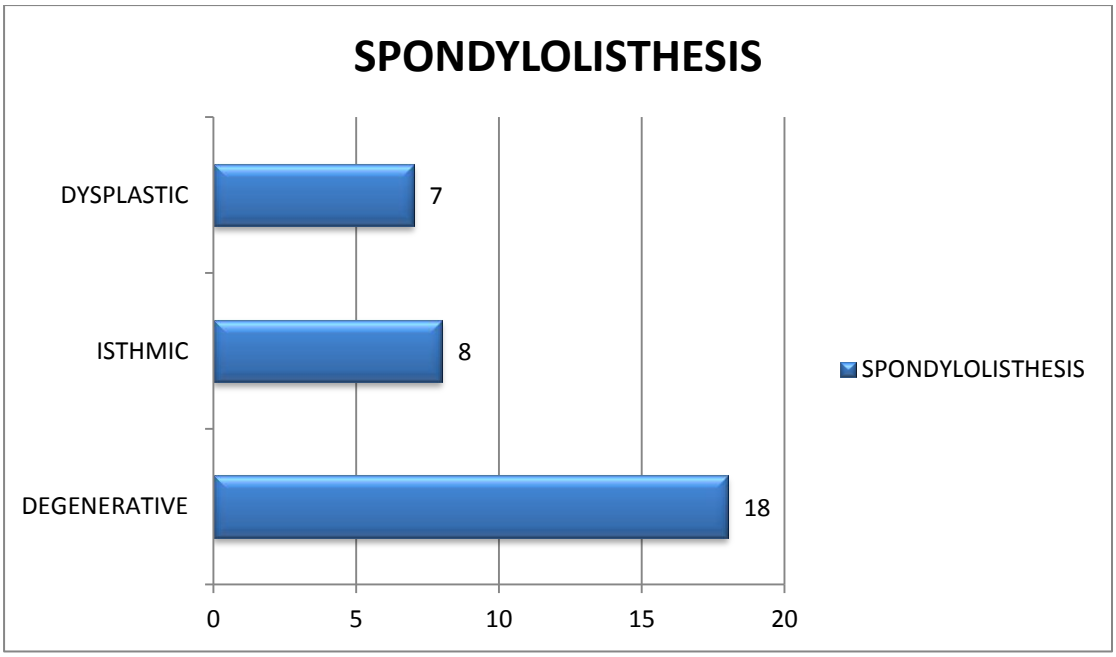

SMOKING HABIT
8
88
SMOKERS
NON-SMOKERS

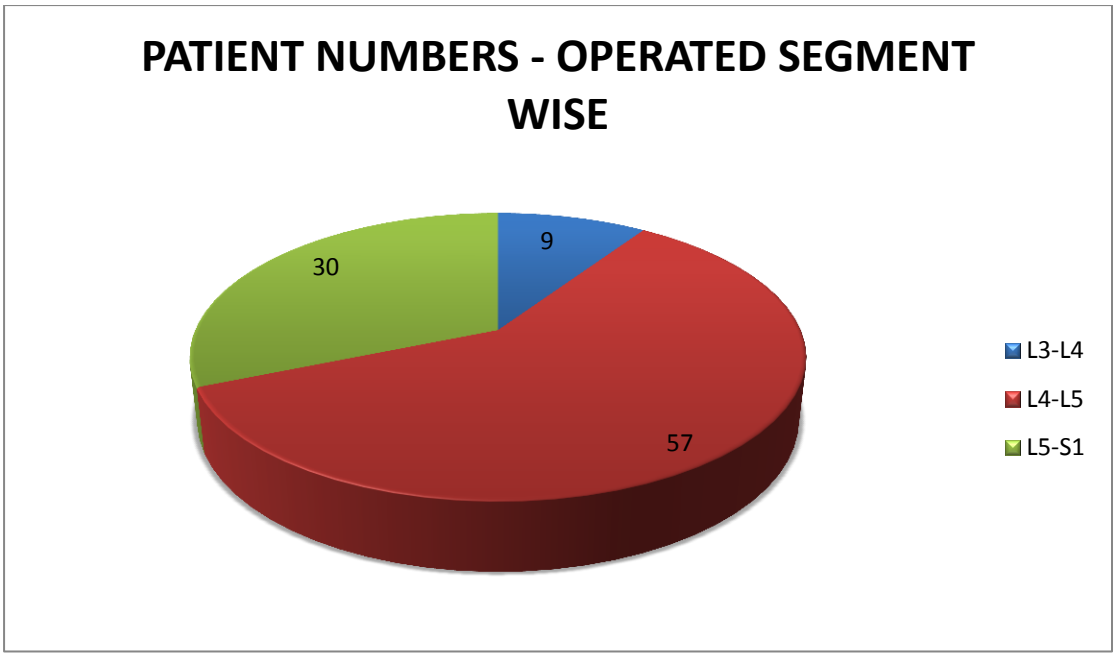

60
50
40
30
20
10
0
57
2
31
6
DISCECTOMY
IPLIF
NONSMOKERS
SMOKERS

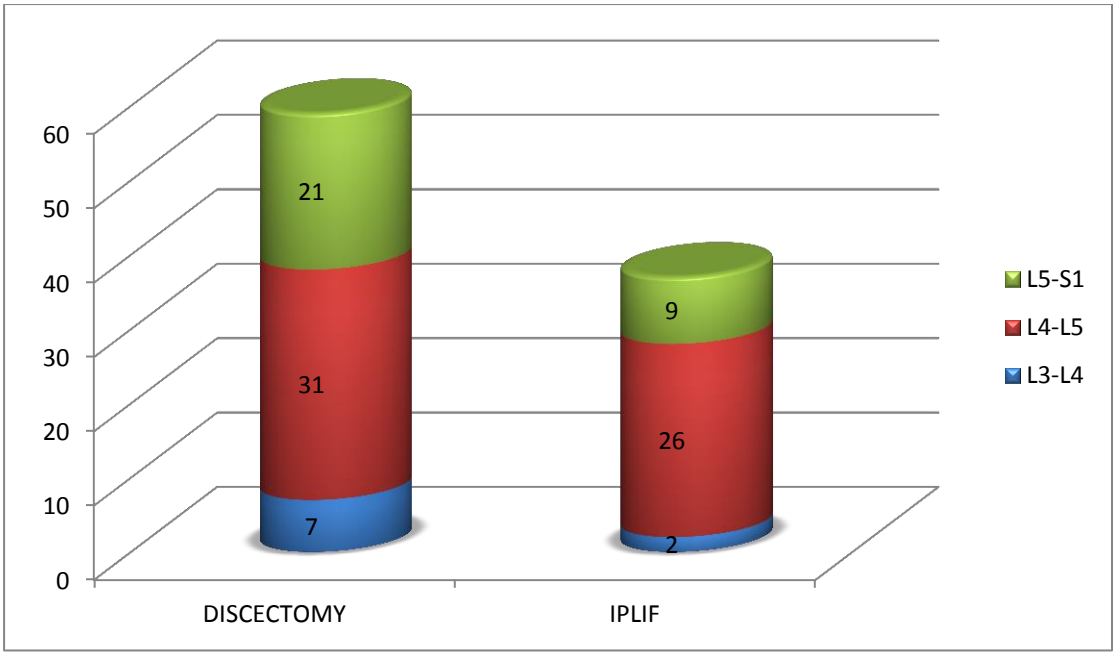

PHYSIOTHERAPY COMPLIANCE
15
41
1
39
REGULAR
IRREGULAR
NOT TAUGHT
UNKNOWN

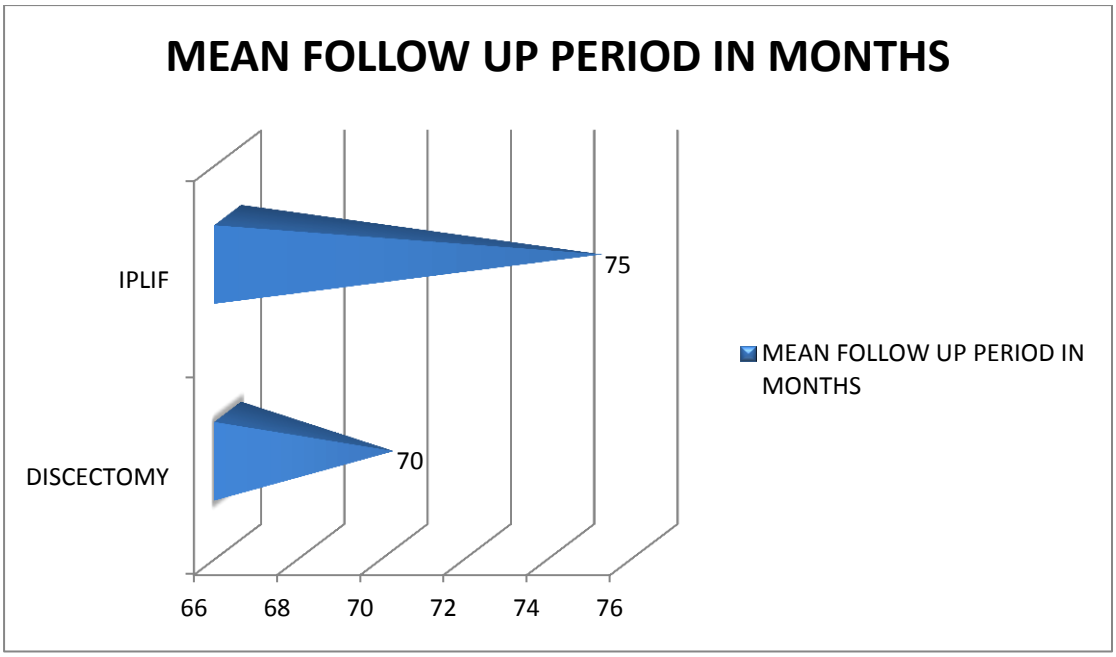

60
50
40
30
20
10
0
24
1
26
8
15
0
15
7
DISCECTOMY
IPLIF
UNKNOWN
NOT TAUGHT
IRREGULAR
REGULAR

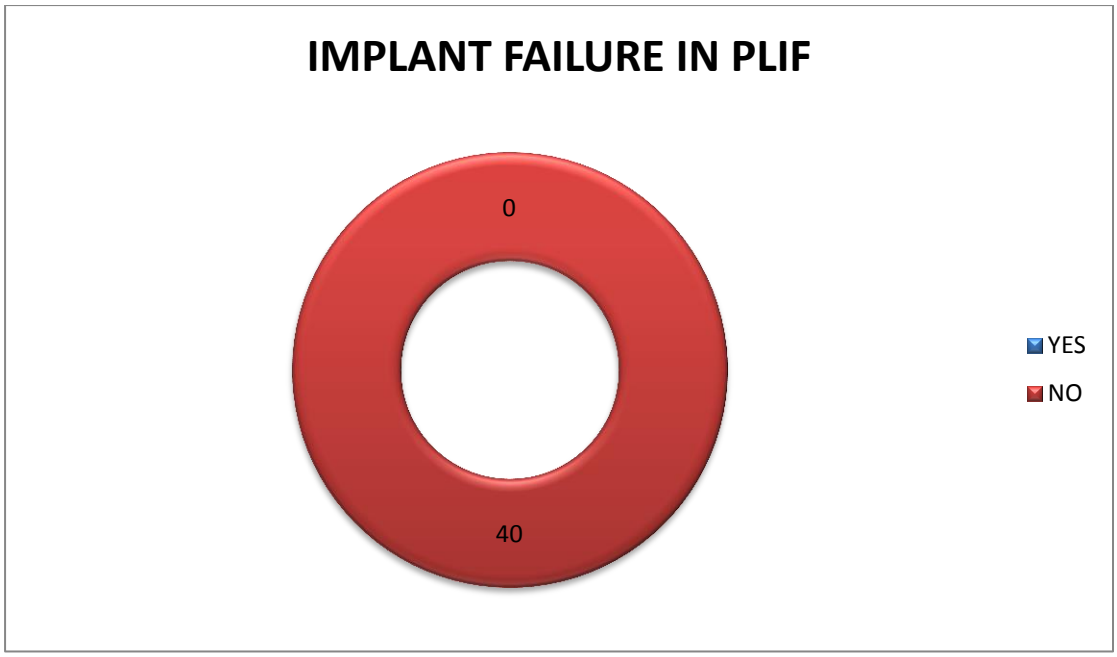

PATIENT NUMBERS - DIAGNOSIS WISE
4
30
62
IVDP
SPONDYLOLISTHESIS
INFECTION

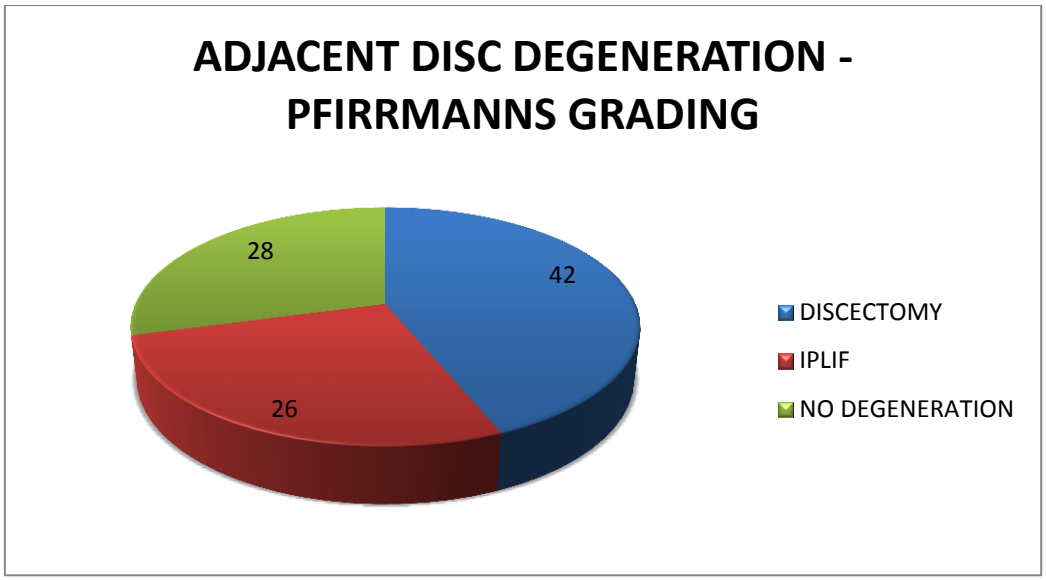

SPONDYLOLISTHESIS
DYSPLASTIC
7
ISTHMIC
8
DEGENERATIVE
18
0
5
10
15
20
SPONDYLOLISTHESIS


PATIENT NUMBERS - OPERATED SEGMENT WISE
9
30
57
L3-L4
L4-L5
L5-S1

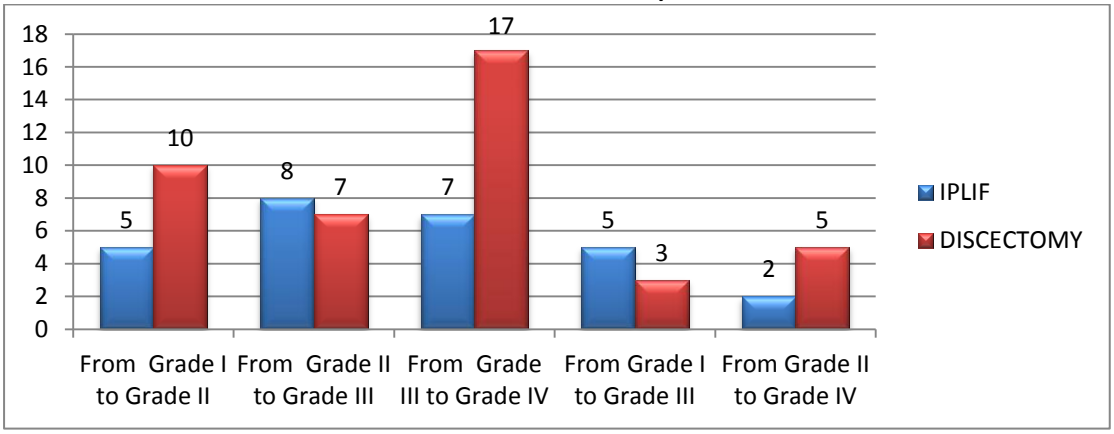

60
50
40
30
20
10
0
21
31
7
9
26
2
DISCECTOMY
IPLIF
L5-S1
L4-L5
L3-L4


MEAN FOLLOW UP PERIOD IN MONTHS
IPLIF
DISCECTOMY
75
70
66
68
70
72
74
76
MEAN FOLLOW UP PERIOD IN MONTHS

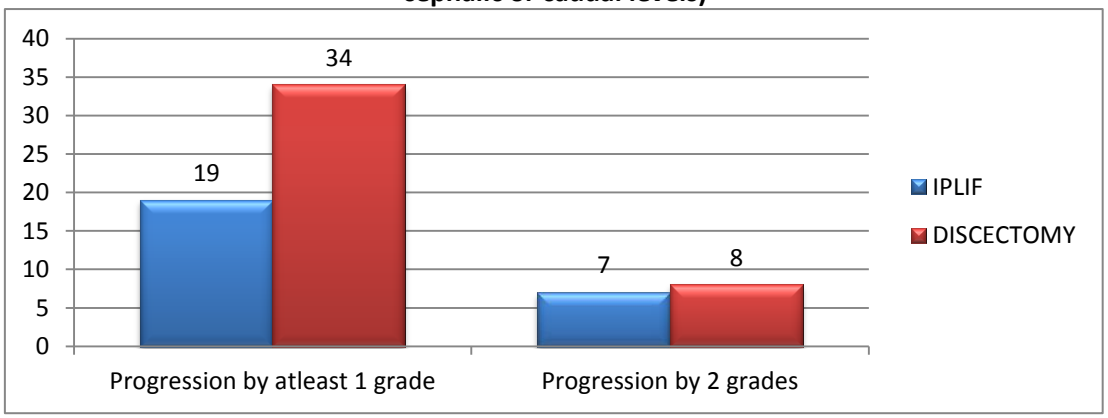

IMPLANT FAILURE IN PLIF
0
40
YES
NO

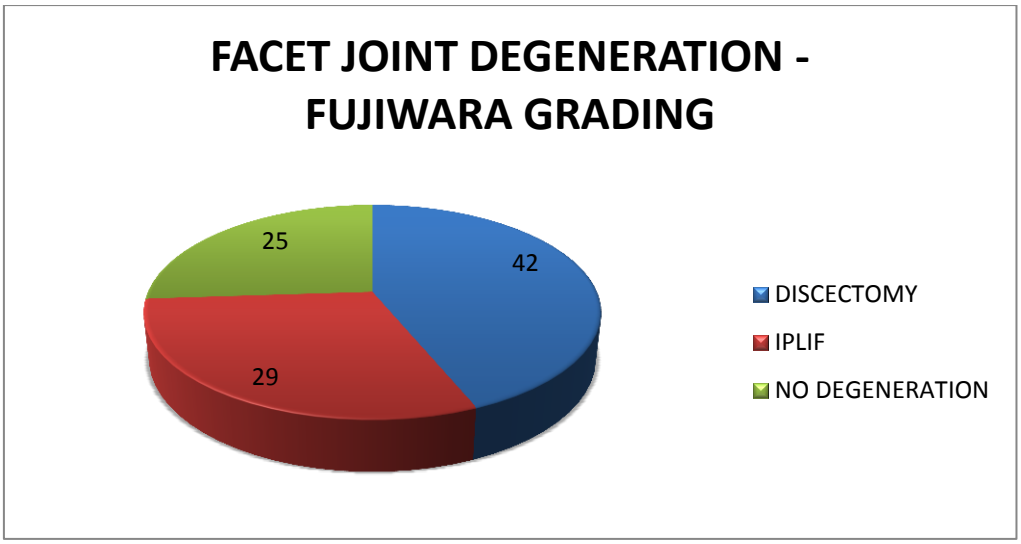


Progression of Degeneration from pre-op to post-op in at least one adjacent disc (cephalic and caudal levels)

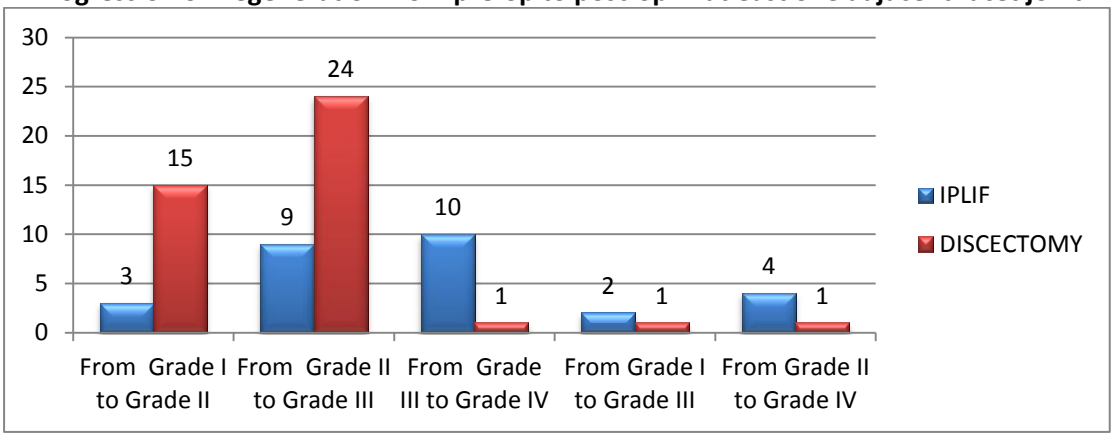


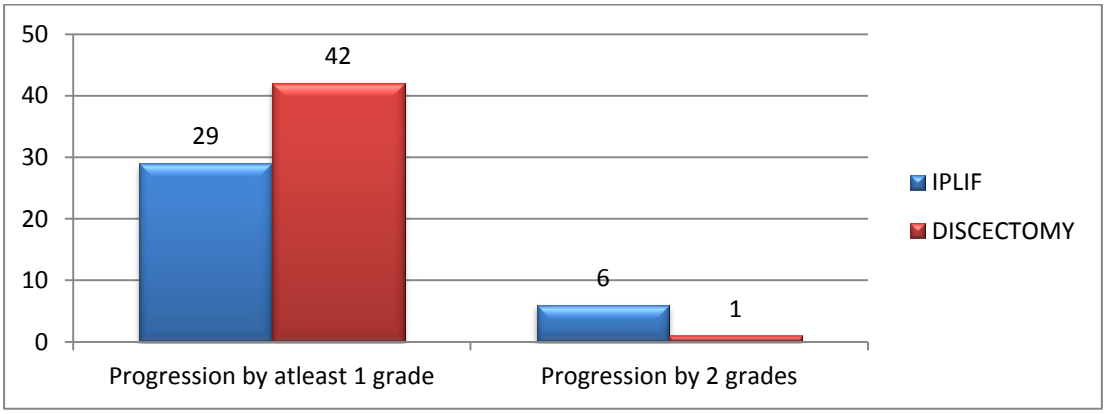
Progression of Degeneration from pre-op to post-op in atleast one adjacent disc (Either cephalic or caudal levels)



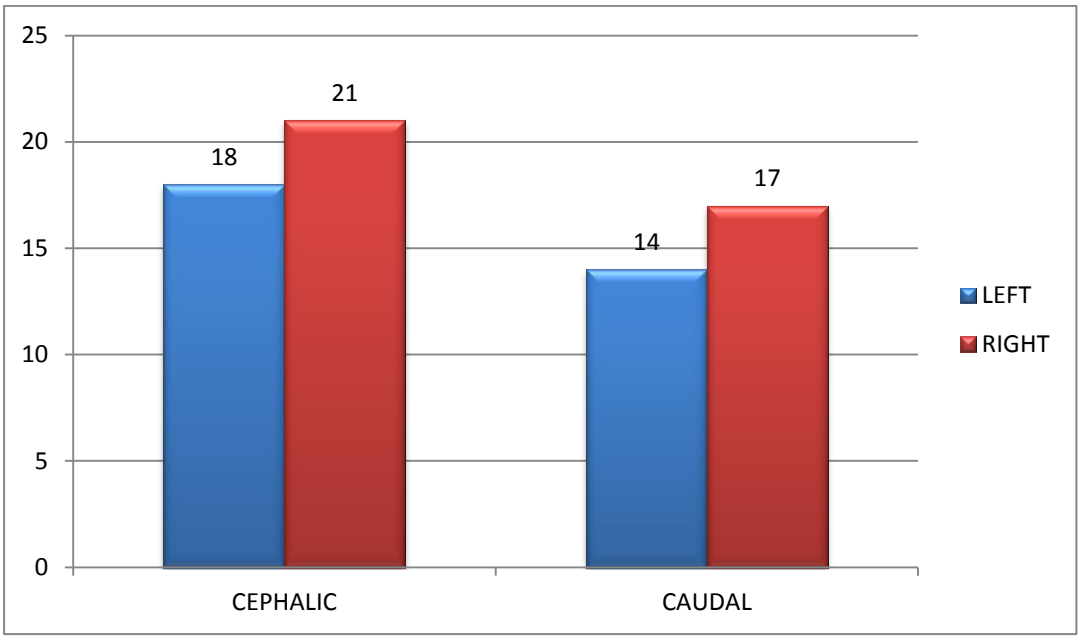


Progression of Degeneration from pre-op to post-op in atleast one adjacent facet joint

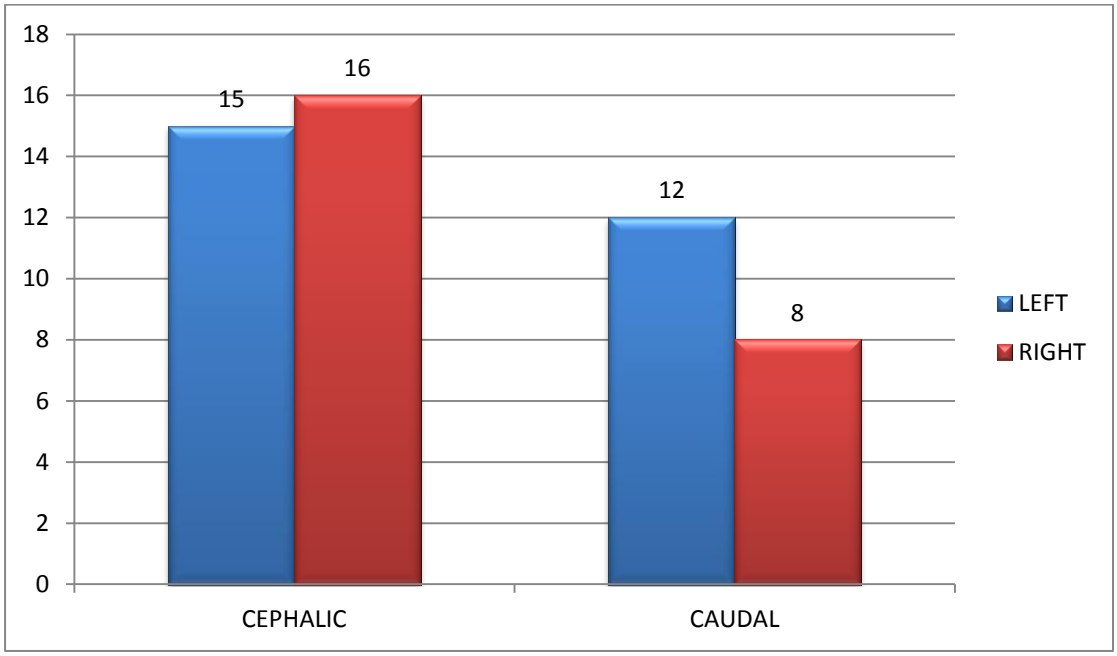




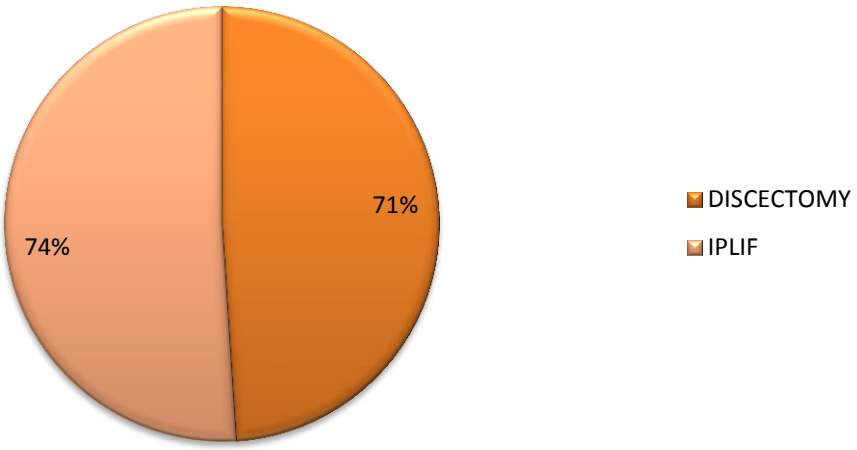
FUJIWARA GRADING OF FACET JOINT DEGENERATION - DISCECTOMY GROUP



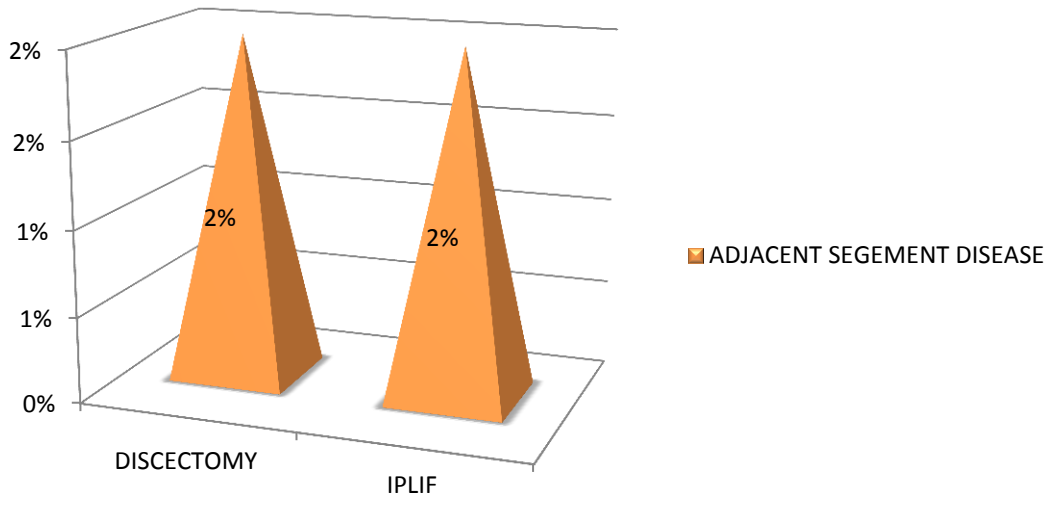
FUJIWARA GRADING OF FACET JOINT DEGENERATION –FUSION GROUP



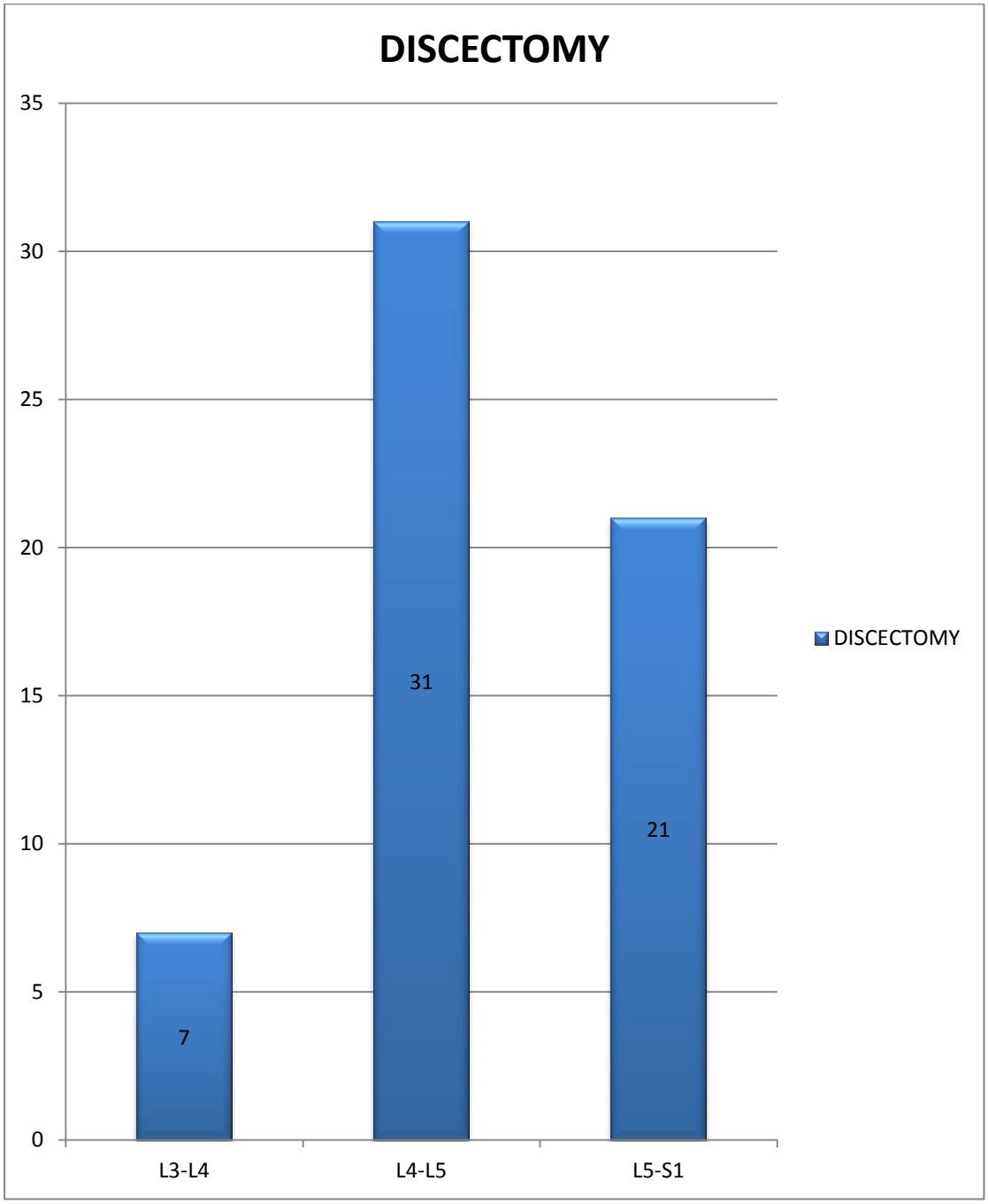
ADJACENT SEGMENT DEGENERATION



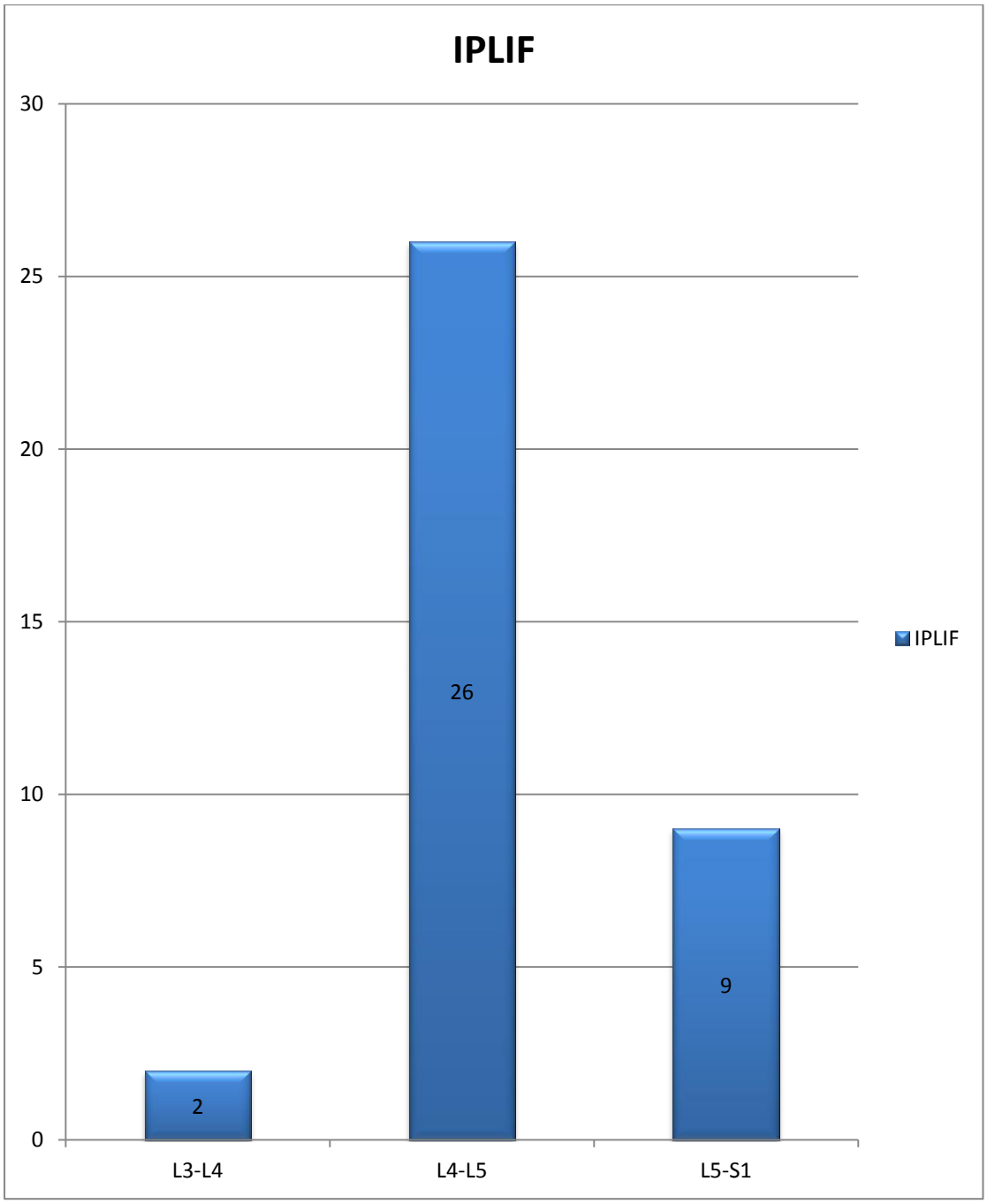
ADJACENT SEGEMENT DISEASE



ADJACENT SEGMENT DEGENERATION – OPERATED SEGMENT WISE

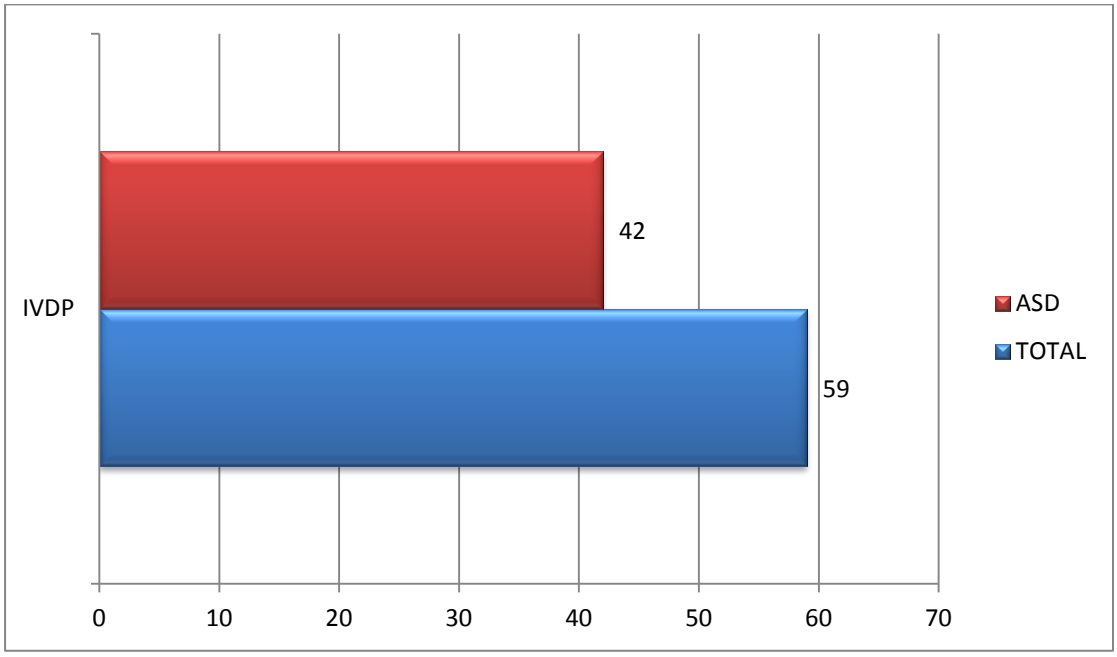


ADJACENT SEGMENT DEGENERATION – OPERATED SEGMENT WISE

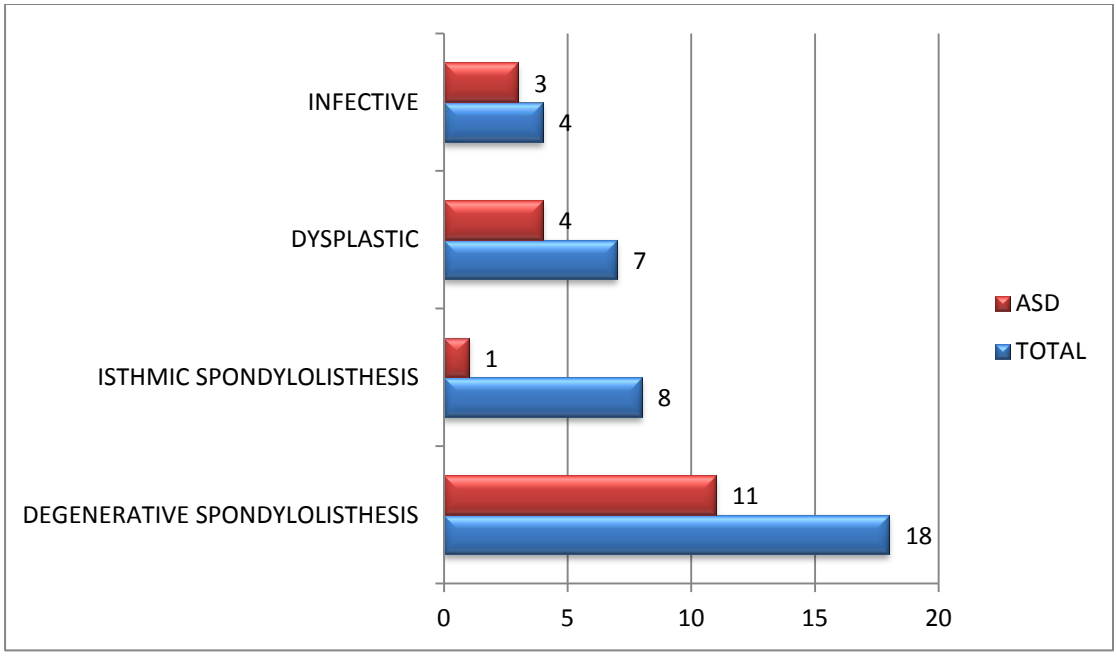


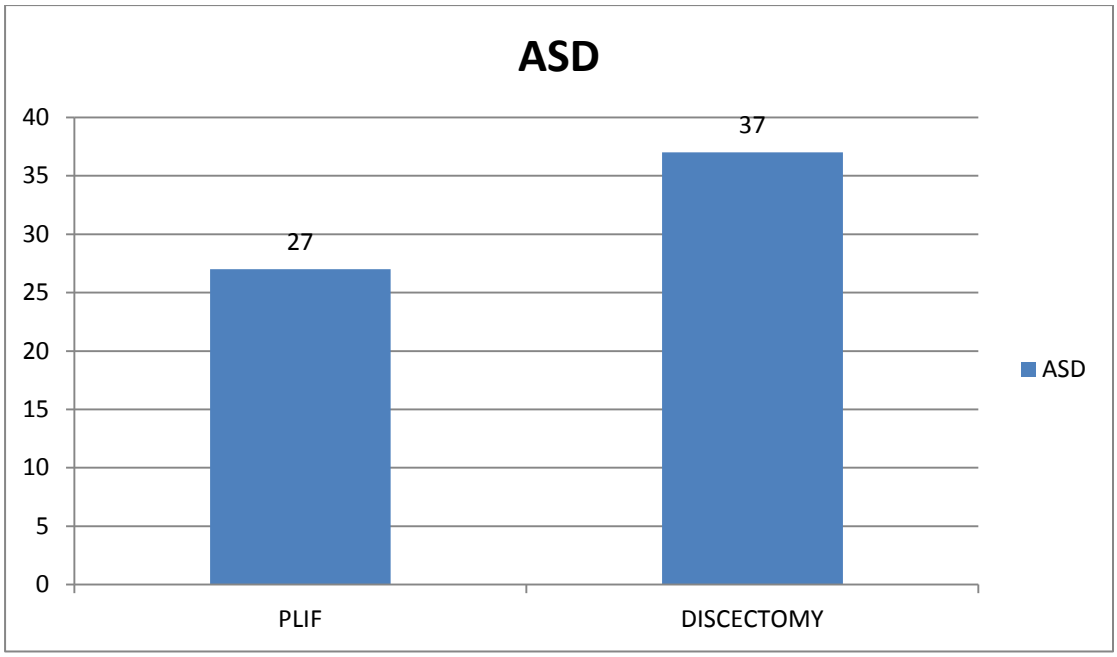
ADJACENT SEGMENT DEGENERATION – DIAGNOSIS WISE

DISCECTOMY GROUP



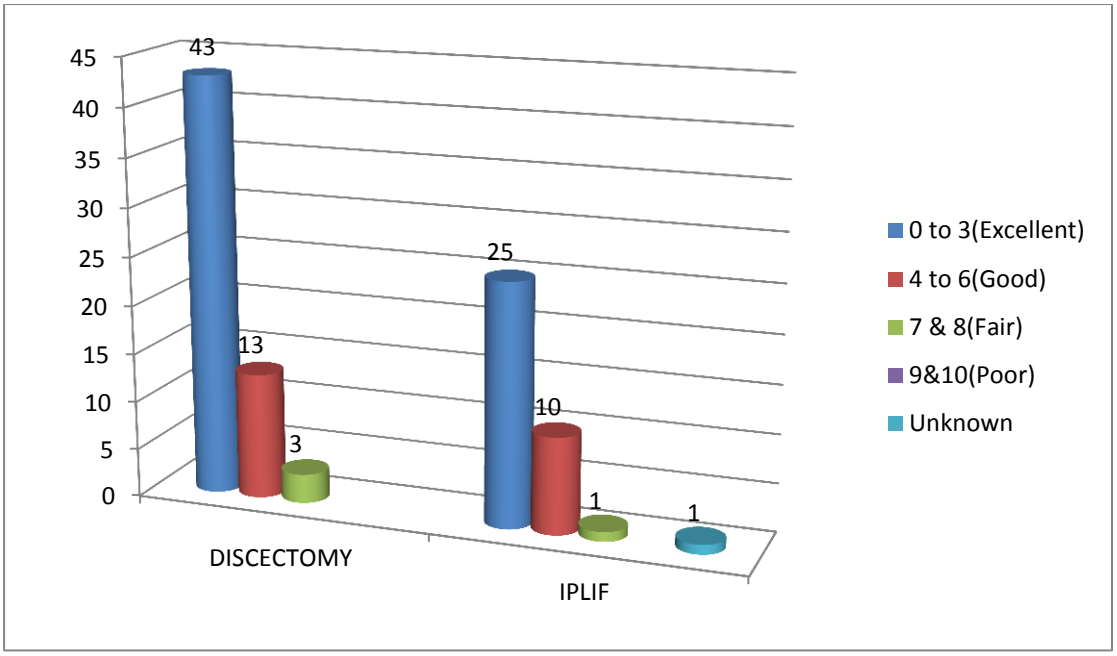
IPLIF GROUP



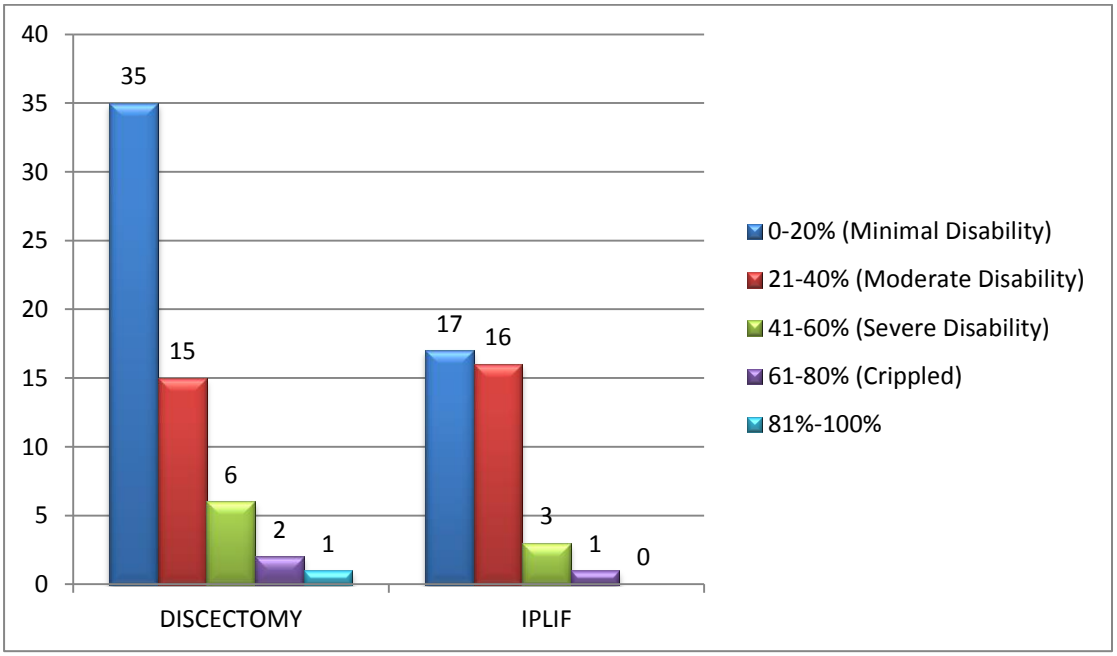

ASD
40
35
30
25
20
15
10
5
0
27
37
PLIF
DISCECTOMY
ASD

FUNCTIONAL OUTCOME MEASURES

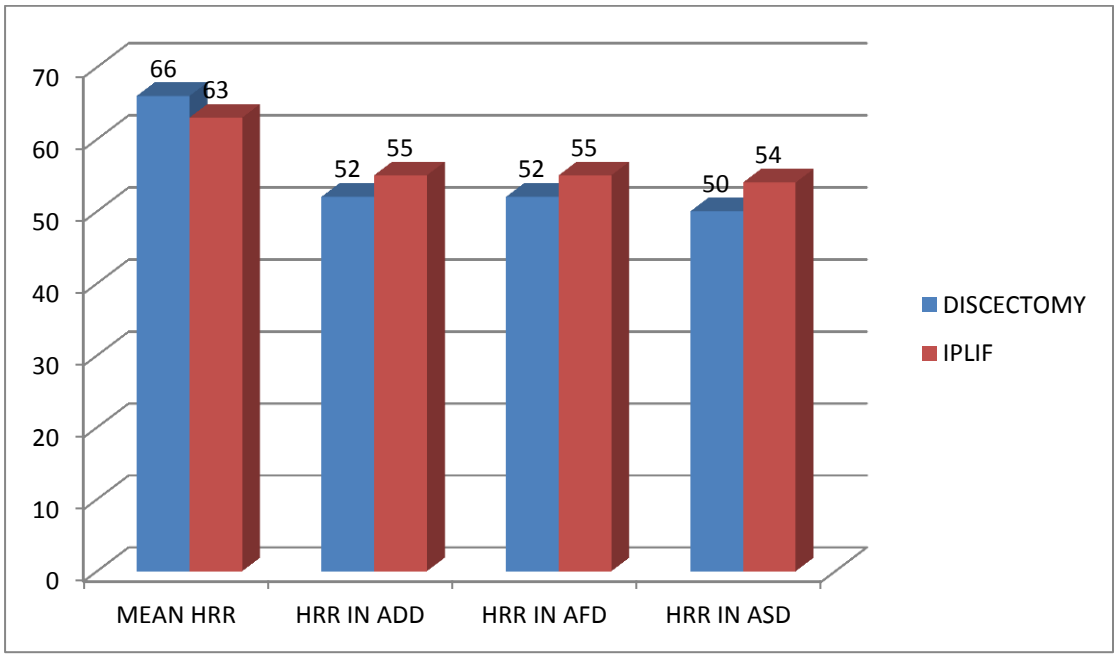
VISUAL ANALOG SCALE



OSWESTRY DISABILITY INDEX



JOA / HIRABIYASHI RECOVERY RATE



ADD-ADJACENT SEGMENT DISC DEGENERATION, AFD-ADJACENT SEGMENT FACET DEGENERATION, ASD- DEGENERATION IN ATLEAST ONE ADJACENT DISC AND ONE ADJACENT FACET

DATA SUMMARY

	Total No.	ASD	
		Degeneration	Disease
DISCECTOMY GROUP			
IVDP	59	24 (41%)	Y
Cauda Equina	1	Y	-
IPLIF GROUP			
Spondylolisthesis	33	16 (43%)	
Degenerative	18	11 (30%)	
Isthmic	8	1 (3%)	Y
Dysplastic	7	4 (57%)	
Grade 1	23	10 (27%)	
Grade 2	8	4 (10%)	Y
Grade 3	1	1 (3%)	
Grade 4	1	1(3%)	
Infective	4	3 (8%)	
Tuberculus	1	1 (3%)	
Pyogenic	3	2 (5%)	

	Total No.	ADD(Pfirrmann Grading)		
		Cephalic	Caudal	Any 1 level
Discectomy	59	35 (59%)	16 (27%)	42 (71%)
IPLIF	37	23 (62%)	13 (35%)	26 (70%)
OVERALL	**96**	**60%**	**30%**	**71%**

	Total No.	AFD(Fujiwara Grading)						
		Cephalic Facet Joints			Caudal Facet Joints			Any 1 facet joint
		Left	Right	Left or Right	Left	Right	Left or Right	
Discectomy	59	18 (31%)	21 (36%)	24 (41%)	14 (24%)	17 (29%)	20 (33%)	42 (71%)
IPLIF	37	15 (41%)	16 (43%)	19 (51%)	12 (32%)	8 (22%)	14 (38%)	29 (78%)
OVERALL	**96**	**34%**	**39%**	**45%**	**27%**	**26%**	**35%**	**74%**

ADD - Adjacent Disc Degeneration, AFD – Adjacent Facet Degeneration, ASD – Adjacent Segment Degeneration, Deg-Degeneration, Dis-Disease

Adjacent Segment Disc and Facet Degeneration			
	Total	**ASDeg**	**ASDis**
Discectomy	**59**	**25 (42%)**	**1 (1.6%)**
L3-4	7	5 (8%)	Nil
L4-5	31	15(25%)	Nil
L5-S1	21	5(8%)	1
IPLIF	**37**	**21 (57%)**	**1 (2.7%)**
L3-4	2	2 (5%)	Nil
L4-5	26	13 (35%)	1
L5-S1	9	6 (16%)	Nil

	Total No.	ASDeg	ASDis
Discectomy	59	42 (71%)	1 (1.6%)
IPLIF	37	27 (74%)	1 (2.7%)
OVERALL	**96**	**69 (72%)**	**2(2%)**

ASDeg-Adjacent Segment Degeneration in one adjacent segment disc and atleast 1 adjacent facet joint, ASDis-Adjacent Segment Disease in the ASDeg group

DISCUSSION

DISCUSSION:

The incidence of adjacent segment degeneration in the study group (IPLIF) was seen in 21(57%) and the incidence of adjacent segment degeneration in the control group (Discectomy) was seen in 25(42%), when considering that there is progression of degeneration by a minimum of 1 grade; compared to the preoperative status, in either the cephalic or caudal adjacent disc and any one of the cephalic or caudal facet joint.

In our study we observed that the incidence of adjacent disc degeneration is more in the cephalic segment in both the discectomy and IPLIF groups, which coincides with the literature findings as described earlier. We also observed that in the facet degeneration a similar pattern exists. The cephalic facet joints seem to be more affected than their caudal counterparts.

While comparing the incidence of adjacent segment degeneration surgical level wise, surgery done at L4-L5 level had the highest incidence of adjacent segment degeneration. Since the number of surgeries at other levels were few statistical analyses was not done. Moreover the incidence of adjacent segment disease was remarkably low in comparison to the degeneration and is on par with the incidence mentioned in the literature.

There were more than 2 grade progression in 7(18%) patients in IPLIF group and 8(13%) patients in discectomy group. This section of patients has the maximum radiographic degeneration, though they comprise a small group. The rest of the

patients with only one grade progression in degeneration are more in number, probably this could be the reason that there is less symptomatic patients in the study considering the point that lesser the radiographic degeneration less is the chance of onset of symptoms.

There appears to be a relationship between smoking and adjacent segment degeneration. The 100% fusion rate which was found in the IPLIF group as per the Kyung Hoon Kim's modification of Brantigan-Steffee classification does not have any correlation with the incidence of adjacent segment degeneration. The discectomy patients were younger than the IPLIF patients at the time of index surgery. Moderate workers were more in both the groups who have adjacent segment degeneration. Male female ratio was reversed in both the groups, females were more in the IPLIF group, while males were more in the discectomy group and this probably is related to the work atmosphere. The physiotherapy compliance was also poor in both the groups, which may be related to the higher incidence of radiological degeneration.

Limitations of the study:

Follow-up is not adequate.

CONCLUSION

Conclusion:

1. Adjacent segment degeneration occurs both in single level discectomy and single level IPLIF surgeries and is marginally more with instrumented fusion.
2. In both groups the cephalic segment is the most affected compared to the caudal segment.
3. There is no significant relationship between radiological degeneration and the clinical adjacent segment disease as claimed by other authors.
4. Since there is only marginal difference, we hold on to our hypothesis that the role of natural degeneration is more compared to the role of instrumented fusion causing adjacent segment degeneration.

BIBLIOGRAPHY

BIBLIOGRAPHY:

1. Andersson GB. Epidemiological features of chronic low-back pain. Lancet. 1999 Aug 14;354(9178):581–5.

2. Van Doorn JW. Low back disability among self-employed dentists, veterinarians, physicians and physical therapists in The Netherlands. A retrospective study over a 13-year period (N = 1,119) and an early intervention program with 1-year follow-up (N = 134). Acta Orthop Scand Suppl. 1995 Jun;263:1–64.

3. C. Schizas, G. Kulik, V. Kosmopoulos. Disc degeneration: Current surgical options. Eur Cell Mater. 2010;vol. 20:306–15.

4. Kallewaard JW, Terheggen MAMB, Groen GJ, Sluijter ME, Derby R, Kapural L, et al. 15. Discogenic low back pain. Pain Pract Off J World Inst Pain. 2010 Dec;10(6):560–79.

5. Chiras J, Morvan G, Merland JJ, Bories J. Blood supply to the thoracic (dorsal) and lumbar spine. Anat Clin. 1982 Mar 1;4(1):23–31.

6. Twomey LT, Taylor JR. Age changes in lumbar vertebrae and intervertebral discs. Clin Orthop. 1987 Nov;(224):97–104.

7. Coventry MB, Ghormley RK, Kernohan JW. The Intervertebral Disc: Its Microscopic Anatomy and Pathology. J Bone Jt Surg. 1945 Jul 1;27(3):460–74.

8. SAUNDERS JM, INMAN VT. PAthology of the intervertebral disk. Arch Surg. 1940 Mar 1;40(3):389–416.

9. Donohue. Pathology of the intervertebral disc. Am J Med Sci. 1939;CXCVIII:419.

10. Roberts S, Menage J, Urban JP. Biochemical and structural properties of the cartilage end-plate and its relation to the intervertebral disc. Spine. 1989 Feb;14(2):166–74.

11. Moore RJ. The vertebral end-plate: what do we know? Eur Spine J Off Publ Eur Spine Soc Eur Spinal Deform Soc Eur Sect Cerv Spine Res Soc. 2000 Apr;9(2):92–6.

12. Broberg KB. On the mechanical behaviour of intervertebral discs. Spine. 1983 Mar;8(2):151–65.

13. Eyre DR. Biochemistry of the intervertebral disc. Int Rev Connect Tissue Res. 1979;8:227–91.

14. Roberts S, Urban JP, Evans H, Eisenstein SM. Transport properties of the human cartilage endplate in relation to its composition and calcification. Spine. 1996 Feb 15;21(4):415–20.

15. V. K. Goel, Y. E. Kim. Effects of injury on the spinal motion segment mechanics in the axial compression mode. Clin Biomech. 1989;vol. 4(no. 3):161–7.

16. Marchand F, Ahmed AM. Investigation of the laminate structure of lumbar disc anulus fibrosus. Spine. 1990 May;15(5):402–10.

17. Johnson EF, Chetty K, Moore IM, Stewart A, Jones W. The distribution and arrangement of elastic fibres in the intervertebral disc of the adult human. J Anat. 1982 Sep;135(Pt 2):301–9.

18. Yu J, Peter C, Roberts S, Urban JP. Elastic fibre organization in the intervertebral discs of the bovine tail. J Anat. 2002 Dec;201(6):465–75.

19. Bruehlmann SB, Rattner JB, Matyas JR, Duncan NA. Regional variations in the cellular matrix of the annulus fibrosus of the intervertebral disc. J Anat. 2002 Aug;201(2):159–71.

20. ERRINGTON RJ, PUUSTJARVI K, WHITE IRF, ROBERTS S, URBAN JPG. Characterisation of cytoplasm-filled processes in cells of the intervertebral disc. J Anat. 1998 Apr;192(Pt 3):369–78.

21. Eyre DR, Muir H. Types I and II collagens in intervertebral disc. Interchanging radial distributions in annulus fibrosus. Biochem J. 1976 Jul 1;157(1):267–70.

22. Eyre, Benya, Buckwalter. The intervertebral disc; basic science perspectives. Am Acad Orthop Surg. 1989;

23. Three-Dimensional Architecture of Lumbar Intervertebral Disc... : Spine [Internet]. [cited 2014 Oct 6]. Available from: http://journals.lww.com/spinejournal/Fulltext/1981/03000/Three_Dimensional_Architecture_of_Lumbar.6.aspx

24. Maroudas A, Stockwell RA, Nachemson A, Urban J. Factors involved in the nutrition of the human lumbar intervertebral disc: cellularity and diffusion of glucose in vitro. J Anat. 1975 Sep;120(Pt 1):113–30.

25. Jazini E, Sharan AD, Morse LJ, Dyke JP, Aronowitz EB, Chen LKH, et al. Alterations in T2 relaxation magnetic resonance imaging of the ovine intervertebral disc due to nonenzymatic glycation. Spine. 2012 Feb 15;37(4):E209–15.

26. Sivan SS, Tsitron E, Wachtel E, Roughley P, Sakkee N, van der Ham F, et al. Age-related accumulation of pentosidine in aggrecan and collagen from normal and degenerate human intervertebral discs. Biochem J. 2006 Oct 1;399(1):29–35.

27. Urban JP, McMullin JF. Swelling pressure of the lumbar intervertebral discs: influence of age, spinal level, composition, and degeneration. Spine. 1988 Feb;13(2):179–87.

28. The Contribution of the Intervertebral Disk to the Scoliotic... : Clinical Orthopaedics and Related Research [Internet]. [cited 2014 Oct 6]. Available from: http://journals.lww.com/corr/Fulltext/1981/05000/The_Contribution_of_the_Intervertebral_Disk_to_the.10.aspx

29. Crock HV, Yoshizawa H, Kame SK. Observations on the venous drainage of the human vertebral body. J Bone Joint Surg Br. 1973 Aug;55(3):528–33.

30. Hassler O. The human intervertebral disc: a micro-angiographical study on its vascular supply at various ages. Acta Orthop. 1969;40(6):765–72.

31. Oki S, Matsuda Y, Shibata T, Okumura H, Desaki J. Morphologic differences of the vascular buds in the vertebral endplate: scanning electron microscopic study. Spine. 1996 Jan 15;21(2):174–7.

32. Urban JP, Holm S, Maroudas A, Nachemson A. Nutrition of the intervertebral disc: effect of fluid flow on solute transport. Clin Orthop. 1982 Oct;(170):296–302.

33. Urban JP, Holm S, Maroudas A. Diffusion of small solutes into the intervertebral disc: as in vivo study. Biorheology. 1978;15(3-4):203–21.

34. Bailey AJ, Paul RG, Knott L. Mechanisms of maturation and ageing of collagen. Mech Ageing Dev. 1998 Dec 1;106(1-2):1–56.

35. Holm S, Maroudas A, Urban JP, Selstam G, Nachemson A. Nutrition of the intervertebral disc: solute transport and metabolism. Connect Tissue Res. 1981;8(2):101–19.

36. Roberts S, Urban JP, Evans H, Eisenstein SM. Transport properties of the human cartilage endplate in relation to its composition and calcification. Spine. 1996 Feb 15;21(4):415–20.

37. Urban MR, Fairbank JC, Etherington PJ, Loh FRCA L, Winlove CP, Urban JP. Electrochemical measurement of transport into scoliotic intervertebral discs in vivo using nitrous oxide as a tracer. Spine. 2001 Apr 15;26(8):984–90.

38. Kauppila LI. Prevalence of stenotic changes in arteries supplying the lumbar spine. A postmortem angiographic study on 140 subjects. Ann Rheum Dis. 1997 Oct;56(10):591–5.

39. Horner HA, Urban JP. 2001 Volvo Award Winner in Basic Science Studies: Effect of nutrient supply on the viability of cells from the nucleus pulposus of the intervertebral disc. Spine. 2001 Dec 1;26(23):2543–9.

40. Stairmand JW, Holm S, Urban JP. Factors influencing oxygen concentration gradients in the intervertebral disc. A theoretical analysis. Spine. 1991 Apr;16(4):444–9.

41. Pooni JS, Hukins DD, Harris PF, Hilton RC, Davies KE. Comparison of the structure of human intervertebral discs in the cervical, thoracic and lumbar regions of the spine. Surg Radiol Anat. 1986 Sep 1;8(3):175–82.

42. Lu YM, Hutton WC, Gharpuray VM. Can variations in intervertebral disc height affect the mechanical function of the disc? Spine. 1996 Oct 1;21(19):2208–16; discussion 2217.

43. Bogduk N, Mercer S. Biomechanics of the cervical spine. I: Normal kinematics. Clin Biomech Bristol Avon. 2000 Nov;15(9):633–48.

44. Watkins R, Watkins R, Williams L, Ahlbrand S, Garcia R, Karamanian A, et al. Stability provided by the sternum and rib cage in the thoracic spine. Spine. 2005 Jun 1;30(11):1283–6.

45. Kulak RF, Belytschko TB, Schultz AB, Galante JO. Nonlinear behavior of the human intervertebral disc under axial load. J Biomech. 1976;9(6):377–86.

46. Macintosh JE, Bogduk N. 1987 Volvo award in basic science. The morphology of the lumbar erector spinae. Spine. 1987 Sep;12(7):658–68.

47. McGill SM, Hughson RL, Parks K. Changes in lumbar lordosis modify the role of the extensor muscles. Clin Biomech Bristol Avon. 2000 Dec;15(10):777–80.

48. Norman R, Wells R, Neumann P, Frank J, Shannon H, Kerr M. A comparison of peak vs cumulative physical work exposure risk factors for the reporting of low back pain in the automotive industry. Clin Biomech Bristol Avon. 1998 Dec;13(8):561–73.

49. Jull G, Amiri M, Bullock-Saxton J, Darnell R, Lander C. Cervical musculoskeletal impairment in frequent intermittent headache. Part 1: Subjects with single headaches. Cephalalgia Int J Headache. 2007 Jul;27(7):793–802.

50. Kong WZ, Goel VK, Gilbertson LG, Weinstein JN. Effects of muscle dysfunction on lumbar spine mechanics. A finite element study based on a two motion segments model. Spine. 1996 Oct 1;21(19):2197–206; discussion 2206–7.

51. Roberts S, Evans H, Trivedi J, Menage J. Histology and Pathology of the Human Intervertebral Disc. J Bone Jt Surg. 2006 Apr 1;88(suppl 2):10–4.

52. Ohshima H, Urban JP, Bergel DH. Effect of static load on matrix synthesis rates in the intervertebral disc measured in vitro by a new perfusion technique. J Orthop Res Off Publ Orthop Res Soc. 1995 Jan;13(1):22–9.

53. Masuda K, An HS. Growth factors and the intervertebral disc. Spine J Off J North Am Spine Soc. 2004 Dec;4(6 Suppl):330S – 340S.

54. Masuda K, Imai Y, Okuma M, Muehleman C, Nakagawa K, Akeda K, et al. Osteogenic protein-1 injection into a degenerated disc induces the restoration of disc height and structural changes in the rabbit anular puncture model. Spine. 2006 Apr 1;31(7):742–54.

55. Thompson JP, Oegema TR, Bradford DS. Stimulation of mature canine intervertebral disc by growth factors. Spine. 1991 Mar;16(3):253–60.

56. Huang K-Y, Yan J-J, Hsieh C-C, Chang M-S, Lin R-M. The in vivo biological effects of intradiscal recombinant human bone morphogenetic protein-2 on the injured intervertebral disc: an animal experiment. Spine. 2007 May 15;32(11):1174–80.

57. Masuda K, Oegema TR, An HS. Growth factors and treatment of intervertebral disc degeneration. Spine. 2004 Dec 1;29(23):2757–69.

58. Adams ME, Billingham ME, Muir H. The glycosaminoglycans in menisci in experimental and natural osteoarthritis. Arthritis Rheum. 1983 Jan;26(1):69–76.

59. Zhang Y, Anderson DG, Phillips FM, Thonar EJ-M, He T-C, Pietryla D, et al. Comparative Effects of Bone Morphogenetic Proteins and Sox9 Overexpression on Matrix Accumulation by Bovine Anulus Fibrosus Cells: Implications for Anular Repair. Spine. 2007 Nov;32(23):2515–20.

60. Maldonado BA, Oegema TR. Initial characterization of the metabolism of intervertebral disc cells encapsulated in microspheres. J Orthop Res Off Publ Orthop Res Soc. 1992 Sep;10(5):677–90.

61. Nagano T, Yonenobu K, Miyamoto S, Tohyama M, Ono K. Distribution of the basic fibroblast growth factor and its receptor gene expression in normal and degenerated rat intervertebral discs. Spine. 1995 Sep 15;20(18):1972–8.

62. Flechtenmacher J, Huch K, Thonar EJ, Mollenhauer JA, Davies SR, Schmid TM, et al. Recombinant human osteogenic protein 1 is a potent stimulator of the synthesis of cartilage proteoglycans and collagens by human articular chondrocytes. Arthritis Rheum. 1996 Nov;39(11):1896–904.

63. Shinmei M, Kikuchi T, Yamagishi M, Shimomura Y. The role of interleukin-1 on proteoglycan metabolism of rabbit annulus fibrosus cells cultured in vitro. Spine. 1988 Nov;13(11):1284–90.

64. Le Maitre CL, Pockert A, Buttle DJ, Freemont AJ, Hoyland JA. Matrix synthesis and degradation in human intervertebral disc degeneration. Biochem Soc Trans. 2007 Aug;35(Pt 4):652–5.

65. Le Maitre CL, Freemont AJ, Hoyland JA, others. The role of interleukin-1 in the pathogenesis of human intervertebral disc degeneration. Arthritis Res Ther. 2005;7(4):R732–45.

66. Kang JD, Stefanovic-Racic M, McIntyre LA, Georgescu HI, Evans CH. Toward a Biochemical Understanding of Human Intervertebral Disc Degeneration and Herniation: Contributions of Nitric Oxide, Interleukins, Prostaglandin E2, and Matrix Metalloproteinases. Spine [Internet]. 1997;22(10). Available from: http://journals.lww.com/spinejournal/Fulltext/1997/05150/Toward_a_Biochemical_Understanding_of_Human.3.aspx

67. Iannone F, Lapadula G. The pathophysiology of osteoarthritis. Aging Clin Exp Res. 2003 Oct;15(5):364–72.

68. Herbert CM, Lindberg KA, Jayson MI, Bailey AJ. Proceedings: Intervertebral disc collagen in degenerative disc disease. Ann Rheum Dis. 1975 Oct;34(5):467.

69. Monnier VM, Kohn RR, Cerami A. Accelerated age-related browning of human collagen in diabetes mellitus. Proc Natl Acad Sci U S A. 1984 Jan;81(2):583–7.

70. Lyons H, Jones E, Quinn FE, Sprunt DH. Changes in the protein-polysaccharide fractions of nucleus pulposus from human intervertebral disc with age and disc herniation. J Lab Clin Med. 1966 Dec;68(6):930–9.

71. Buckwalter JA, Roughley PJ, Rosenberg LC. Age-Related changes in cartilage proteoglycans: Quantitative electron microscopic studies. Microsc Res Tech. 1994 Aug 1;28(5):398–408.

72. Buckwalter JA, Woo SL, Goldberg VM, Hadley EC, Booth F, Oegema TR, et al. Soft-tissue aging and musculoskeletal function. J Bone Joint Surg Am. 1993 Oct;75(10):1533–48.

73. R S, M A, P R, J M. Aggrecan degradation in human intervertebral disc and articular cartilage [Internet]. 1997 [cited 2014 Oct 8]. Available from: http://www.biochemj.org/bj/326/bj3260235.htm

74. 1988 Volvo Award in Basic Science: Proteoglycan Synthesis in... : Spine [Internet]. [cited 2014 Oct 8]. Available from: http://journals.lww.com/spinejournal/Fulltext/1988/09000/1988_Volvo_Award_in_Basic_Science__Proteoglycan.3.aspx

75. Kim K-W, Kim Y-S, Ha K-Y, Woo Y-K, Park J-B, Park W-S, et al. An autocrine or paracrine Fas-mediated counterattack: a potential mechanism for apoptosis of notochordal cells in intact rat nucleus pulposus. Spine. 2005 Jun 1;30(11):1247–51.

76. Pollintine P, van Tunen MSLM, Luo J, Brown MD, Dolan P, Adams MA. Time-dependent compressive deformation of the ageing spine: relevance to spinal stenosis. Spine. 2010 Feb 15;35(4):386–94.

77. Urban JP, Roberts S. Development and degeneration of the intervertebral discs. Mol Med Today. 1995 Oct;1(7):329–35.

78. Urban JPG, Smith S, Fairbank JCT. Nutrition of the Intervertebral Disc: Spine. 2004 Dec;29(23):2700–9.

79. Battié MC, Videman T, Levälahti E, Gill K, Kaprio J. Genetic and environmental effects on disc degeneration by phenotype and spinal level: a multivariate twin study. Spine. 2008 Dec 1;33(25):2801–8.

80. Patel AA, Spiker WR, Daubs M, Brodke D, Cannon-Albright LA. Evidence for an inherited predisposition to lumbar disc disease. J Bone Joint Surg Am. 2011 Feb 2;93(3):225–9.

81. Videman T, Leppävuori J, Kaprio J, Battié MC, Gibbons LE, Peltonen L, et al. Intragenic polymorphisms of the vitamin D receptor gene associated with intervertebral disc degeneration. Spine. 1998 Dec 1;23(23):2477–85.

82. Kales SN, Linos A, Chatzis C, Sai Y, Halla M, Nasioulas G, et al. The Role of Collagen IX Tryptophan Polymorphisms in Symptomatic Intervertebral Disc Disease in Southern European Patients. Spine [Internet]. 2004;29(11). Available from: http://journals.lww.com/spinejournal/Fulltext/2004/06010/The_Role_of_Collagen_IX_Tryptophan_Polymorphisms.17.aspx

83. Mio F, Chiba K, Hirose Y, Kawaguchi Y, Mikami Y, Oya T, et al. A functional polymorphism in COL11A1, which encodes the alpha 1 chain of type XI collagen,

is associated with susceptibility to lumbar disc herniation. Am J Hum Genet. 2007 Dec;81(6):1271–7.

84. Min S-K, Nakazato K, Yamamoto Y, Gushiken K, Fujimoto H, Fujishiro H, et al. Cartilage intermediate layer protein gene is associated with lumbar disc degeneration in male, but not female, collegiate athletes. Am J Sports Med. 2010 Dec;38(12):2552–7.

85. Solovieva S, Noponen N, Männikkö M, Leino-Arjas P, Luoma K, Raininko R, et al. Association Between the Aggrecan Gene Variable Number of Tandem Repeats Polymorphism and Intervertebral Disc Degeneration. Spine [Internet]. 2007;32(16). Available from: http://journals.lww.com/spinejournal/Fulltext/2007/07150/Association_Between_the_Aggrecan_Gene_Variable.3.aspx

86. Dong DM, Yao M, Liu B, Sun CY, Jiang YQ, Wang YS. Association between the -1306C/T polymorphism of matrix metalloproteinase-2 gene and lumbar disc disease in Chinese young adults. Eur Spine J. 2007 Nov;16(11):1958–61.

87. Videman T, Saarela J, Kaprio J, Näkki A, Levälahti E, Gill K, et al. Associations of 25 structural, degradative, and inflammatory candidate genes with lumbar disc desiccation, bulging, and height narrowing. Arthritis Rheum. 2009 Feb;60(2):470–81.

88. Andersen S, Skorpen F. Variation in the COMT gene: implications for pain perception and pain treatment. Pharmacogenomics. 2009 Apr 1;10(4):669–84.

89. Cuellar JM, Golish SR, Reuter MW, Cuellar VG, Angst MS, Carragee EJ, et al. Cytokine evaluation in individuals with low back pain using discographic lavage. Spine J. 10(3):212–8.

90. Kroeber MW, Unglaub F, Wang H, Schmid C, Thomsen M, Nerlich A, et al. New in vivo animal model to create intervertebral disc degeneration and to investigate the effects of therapeutic strategies to stimulate disc regeneration. Spine. 2002 Dec 1;27(23):2684–90.

91. Le Maitre CL, Freemont AJ, Hoyland JA. Localization of degradative enzymes and their inhibitors in the degenerate human intervertebral disc. J Pathol. 2004 Sep;204(1):47–54.

92. Le Maitre CL, Freemont AJ, Hoyland JA. The role of interleukin-1 in the pathogenesis of human Intervertebral disc degeneration. Arthritis Res Ther. 2005;7(4):R732–45.

93. Studer RK, Vo N, Sowa G, Ondeck C, Kang J. Human Nucleus Pulposus Cells React to IL-6: Independent Actions and Amplification of Response to IL-1 and TNF-α. Spine. 2011 Apr;36(8):593–9.

94. Séguin CA, Pilliar RM, Roughley PJ, Kandel RA. Tumor necrosis factor-alpha modulates matrix production and catabolism in nucleus pulposus tissue. Spine. 2005 Sep 1;30(17):1940–8.

95. Weiler C, Nerlich AG, Bachmeier BE, Boos N. Expression and Distribution of Tumor Necrosis Factor Alpha in Human Lumbar Intervertebral Discs: A Study in Surgical Specimen and Autopsy Controls. Spine [Internet]. 2005;30(1). Available from: http://journals.lww.com/spinejournal/Fulltext/2005/01010/Expression_and_Distribution_of_Tumor_Necrosis.9.aspx

96. Peng B, Hao J, Hou S, Wu W, Jiang D, Fu X, et al. Possible pathogenesis of painful intervertebral disc degeneration. Spine. 2006 Mar 1;31(5):560–6.

97. Lee JM, Song JY, Baek M, Jung H-Y, Kang H, Han IB, et al. Interleukin-1β induces angiogenesis and innervation in human intervertebral disc degeneration. J Orthop Res Off Publ Orthop Res Soc. 2011 Feb;29(2):265–9.

98. Kim JH, Studer RK, Sowa GA, Vo NV, Kang JD. Activated macrophage-like THP-1 cells modulate anulus fibrosus cell production of inflammatory mediators in response to cytokines. Spine. 2008 Oct 1;33(21):2253–9.

99. Abe Y, Akeda K, An HS, Aoki Y, Pichika R, Muehleman C, et al. Proinflammatory cytokines stimulate the expression of nerve growth factor by human intervertebral disc cells. Spine. 2007 Mar 15;32(6):635–42.

100. Woolf CJ, Allchorne A, Safieh-Garabedian B, Poole S. Cytokines, nerve growth factor and inflammatory hyperalgesia: the contribution of tumour necrosis factor α. Br J Pharmacol. 1997 May;121(3):417–24.

101. Revell PA, al-Saffar N, Fish S, Osei D. Extracellular matrix of the synovial intimal cell layer. Ann Rheum Dis. 1995 May;54(5):404–7.

102. Bondeson J, Blom AB, Wainwright S, Hughes C, Caterson B, van den Berg WB. The role of synovial macrophages and macrophage-produced mediators in driving inflammatory and destructive responses in osteoarthritis. Arthritis Rheum. 2010 Mar 1;62(3):647–57.

103. Sowa G. Facet-mediated pain. Dis--Mon DM. 2005 Jan;51(1):18–33.

104. Adams MA, Hutton WC. The effect of posture on the role of the apophysial joints in resisting intervertebral compressive forces. J Bone Joint Surg Br. 1980 Aug;62(3):358–62.

105. Aigner T, Stöve J. Collagens--major component of the physiological cartilage matrix, major target of cartilage degeneration, major tool in cartilage repair. Adv Drug Deliv Rev. 2003 Nov 28;55(12):1569–93.

106. Suri S, Gill SE, de Camin SM, Wilson D, McWilliams DF, Walsh DA. Neurovascular invasion at the osteochondral junction and in osteophytes in osteoarthritis. Ann Rheum Dis. 2007 Nov;66(11):1423–8.

107. Igarashi A, Kikuchi S, Konno S. Correlation between inflammatory cytokines released from the lumbar facet joint tissue and symptoms in degenerative lumbar spinal disorders. J Orthop Sci Off J Jpn Orthop Assoc. 2007 Mar;12(2):154–60.

108. Caron JP, Fernandes JC, Martel-Pelletier J, Tardif G, Mineau F, Geng C, et al. Chondroprotective effect of intraarticular injections of interleukin-1 receptor antagonist in experimental osteoarthritis. Suppression of collagenase-1 expression. Arthritis Rheum. 1996 Sep;39(9):1535–44.

109. Valat J-P, Genevay S, Marty M, Rozenberg S, Koes B. Sciatica. Best Pract Res Clin Rheumatol. 2010 Apr;24(2):241–52.

110. Olmarker K, Rydevik B, Nordborg C. Autologous Nucleus Pulposus Induces Neurophysiologic and Histologic Changes in Porcine Cauda Equina Nerve Roots. Spine [Internet]. 1993;18(11). Available from: http://journals.lww.com/spinejournal/Fulltext/1993/09010/Autologous_Nucleus_Pulposus_Induces.5.aspx

111. Olmarker K, Rydevik B. Selective Inhibition of Tumor Necrosis Factor-α Prevents Nucleus Pulposus-Induced Thrombus Formation, Intraneural Edema, and Reduction of Nerve Conduction Velocity: Possible Implications for Future Pharmacologic Treatment Strategies of Sciatica. Spine [Internet]. 2001;26(8). Available from: http://journals.lww.com/spinejournal/Fulltext/2001/04150/Selective_Inhibition_of_Tumor_Necrosis_Factor__.7.aspx

112. Olmarker K, Larsson K. Tumor Necrosis Factor α and Nucleus-Pulposus-Induced Nerve Root Injury. Spine [Internet]. 1998;23(23). Available from: http://journals.lww.com/spinejournal/Fulltext/1998/12010/Tumor_Necrosis_Factor___and.8.aspx

113. Yabuki S, Kikuchi S, Olmarker K, Myers RR. Acute Effects of Nucleus Pulposus on Blood Flow and Endoneurial Fluid Pressure in Rat Dorsal Root Ganglia. Spine [Internet]. 1998;23(23). Available from: http://journals.lww.com/spinejournal/Fulltext/1998/12010/Acute_Effects_of_Nucleus_Pulposus_on_Blood_Flow.6.aspx

114. Wagner R, Myers RR. Endoneurial injection of TNF-alpha produces neuropathic pain behaviors. Neuroreport. 1996 Nov 25;7(18):2897–901.

115. Kobayashi S, Baba H, Uchida K, Kokubo Y, Kubota C, Yamada S, et al. Effect of Mechanical Compression on the Lumbar Nerve Root: Localization and Changes of Intraradicular Inflammatory Cytokines, Nitric Oxide, and Cyclooxygenase. Spine [Internet]. 2005;30(15). Available from: http://journals.lww.com/spinejournal/Fulltext/2005/08010/Effect_of_Mechanical_Compression_on_the_Lumbar.4.aspx

116. Omarker K, Myers RR. Pathogenesis of sciatic pain: role of herniated nucleus pulposus and deformation of spinal nerve root and dorsal root ganglion. Pain. 1998 Nov;78(2):99–105.

117. Jacobs LJ, Vo N, Kang JD. Identifying Inflammatory Targets for Biologic Therapies for Spine Pain. PM&R. 2011 Jun;3(6, Supplement):S12–7.

118. Inufusa A, An HS, Lim TH, Hasegawa T, Haughton VM, Nowicki BH. Anatomic changes of the spinal canal and intervertebral foramen associated with flexion-extension movement. Spine. 1996 Nov 1;21(21):2412–20.

119. Kosaka H, Sairyo K, Biyani A, Leaman D, Yeasting R, Higashino K, et al. Pathomechanism of Loss of Elasticity and Hypertrophy of Lumbar Ligamentum Flavum in Elderly Patients With Lumbar Spinal Canal Stenosis: Spine. 2007 Dec;32(25):2805–11.

120. Nakatani T, Marui T, Hitora T, Doita M, Nishida K, Kurosaka M. Mechanical stretching force promotes collagen synthesis by cultured cells from human ligamentum flavum via transforming growth factor-β1. J Orthop Res. 2002 Nov 1;20(6):1380–6.

121. Roughley PJ. Biology of intervertebral disc aging and degeneration: involvement of the extracellular matrix. Spine. 2004 Dec 1;29(23):2691–9.

122. K. J. Schnake, M. Putzier, N. P. Haas, F. Kandziora. Mechanical concepts for disc regeneration. Eur Spine J. 2006;15(3):S354–60.

123. P. P. Raj. Inter vertebral disc: anatomy-physiology-patho physiology-treatment,. Pain Pract. 2008;8(1):18–44.

124. M. A. Adams, P. J. Roughley. What is intervertebral disc degeneration, and what causes it? Spine. 2006;31(18):2151–61.

125. J. P. G. Urban, S. Roberts. Degeneration of the intervertebral disc. Arthritis Res Ther. 2003;5(3):120–30.

126. Amonoo-Kuofi HS. Morphometric changes in the heights and anteroposterior diameters of the lumbar intervertebral discs with age. J Anat. 1991 Apr;175:159–68.

127. H. S. An, P. A. Anderson, V. M. Haughton. Introduction. Disc degeneration: summary. Spine. 2004;29(23):2677–8.

128. Miller JAA, Schmatz C, Schultz AB. Lumbar disc degeneration: correlation with age, sex, and spine level in 600 autopsy specimens. Spine. 1988;13:173–8.

129. Lawrence JS. Disc degeneration. Its frequency and relationship to symptoms. Ann Rheum Dis. 1969;28(2):121–38.

130. Michele C. Battie, Tapio Videman, DrMedSci, Eric Parent. Lumbar Disc Degeneration. Spine. 2004;29(23):2679–90.

131. Siemionow K, An H, Masuda K, Andersson G, Cs-Szabo G. The Effects of Age, Sex, Ethnicity, and Spinal Level on the Rate of Intervertebral Disc Degeneration: A Review of 1712 Intervertebral Discs. Spine. 2011 Aug;36(17):1333–9.

132. Kelsey JL, White AA. Epidemiology and impact on low back pain. Spine. 1980;5:133–42.

133. H. J. Wilke, P. Neef, M. Caimi, T. Hoogland, L. E. Claes. New in vivo measurements of pressures in the intervertebral disc in daily life. Spine. 1999;24(8):755–62.

134. F. Heuer, H. Schmidt, H. J.Wilke. The relation between intervertebral disc bulging and annular fiber associated strains for simple and complex loading. J Biomech. 2008;41(5):1086–94.

135. M. A. Adams, D. S. McNally, P. Dolan. Stress distributions inside intervertebral discs. The effects of age and degeneration. J Bone Jt Surgery—Series B. 1996;78(6):965–72.

136. H. J.Wilke, F. Rohlmann, C. Neidlinger-Wilke, K.Werner, L. Claes, A. Kettler. Validity and interobserver agreement of a new radiographic grading system for intervertebral disc degeneration: part I. Lumbar spine. Eur Spine J. 2006;15(6):720–30.

137. H. Schmidt, A. Kettler, A. Rohlmann, L. Claes, H. J., Wilke. The risk of disc prolapses with complex loading in different degrees of disc degeneration—a finite element analysis. Clin Biomech. 2007;22(9):988–98.

138. Palepu V, Kodigudla M, Goel VK. Biomechanics of Disc Degeneration. Adv Orthop. 2012;2012:1–17.

139. W. Z. Kong, V. K. Goel, L. G. Gilbertson, J. N.Weinstein. Effects of muscle dysfunction on lumbar spine mechanics: a finite element study based on a two motion segments model. Spine. 1996;21(19):2197–207.

140. Dunlop RB, Adams MA, Hutton WC. Disc space narrowing and the lumbar facet joints. J Bone Jt Surg Br. 1984;66:706–10.

141. S. Wang, Q. Xia, P. Passias, W. Li, K. Wood, G. Li. How does lumbar degenerative disc disease affect the disc deformation at the cephalic levels in vivo? Spine. 2011;36(9):E574–81.

142. Gotfried Y, Bradford DS, Oegema TR. Facet joint changes after chemonucleolysis-induced disc space narrowing. Spine. 11:944–50.

143. Lipson SJ, Muir H. Experimental intervertebral disc degeneration: morphologic and proteoglycan changes over time. Arthritis Rheum. 1981;24:12–21.

144. Oegema TR, Bradford DS. The inter-relationship of facet joint osteoarthritis and degenerative disc disease. Br J Rheumatol. 1991;30(Suppl 1):16–20.

145. Vernon-Roberts B, Pirie CJ. Degenerative changes in the intervertebral discs of the lumbar spine and their sequelae. Rheumatol Rehabil. 1977;16:13–21.

146. Fujiwara A, Tamai K, Yamato M, An HS, Yoshida H, Saotome K, et al. The relationship between facet joint osteoarthritis and disc degeneration of the lumbar spine: an MRI study. Eur Spine J. 1999;8(5):396–401.

147. Fujiwara A, Lim T-H, An HS, Tanaka N, Jeon C-H, Andersson GB, et al. The effect of disc degeneration and facet joint osteoarthritis on the segmental flexibility of the lumbar spine. Spine. 2000;25(23):3036–44.

148. C. Schizas, G. Kulik, V. Kosmopoulos. Disc degeneration: current surgical options. Eur Cell Mater. 2010;20:306–15.

149. H. J. Wilke, K. Wenger, L. Claes. Testing criteria for spinal implants: recommendations for the standardization of in vitro stability testing of spinal implants. Eur Spine J. 1998;7(2):148–54.

150. V. K. Goel, N. A. Thomas, C. R. Charles, N. K.Weinstein, N. James. A technique to evaluate an internal spinal device by use of the selspot system: an application to luque closed loop. Spine. 1987;12(2):150–9.

151. V. K. Goel, D. G. Wilder, M. H. Pope, W. T. Edwards, R. F. McLain, S. D. Boden. Biomechanical testing of the spine: load-controlled versus displacement-controlled analysis. Spine. 1995;20(21):2354–7.

152. J. C. Wang, P. V. Mummaneni, R. W. Haid. Current treatment strategies for the painful lumbar motion segment: posterolateral fusion versus interbody fusion. Spine. 2005;30(16):S33–43.

153. J. C. Wang, R. W. Haid Jr, J. S. Miller, J. C. Robinson. Comparison of CD HORIZON SPIRE spinous process plate system stabilization and pedicle screw fixation after anterior lumbar interbodyfusion: invited submission from the Joint Section Meeting on Disorders of the Spine and Peripheral Nerves. J Neurosurg. 2006;4:160–4.

154. Jutte, Castelein. Complications of pedicle screws in lumbar and lumbosacral fusions in 105 consecutive primary operations. Eur Spine J. 2002;11:594–8.

155. McAfee PC, Weiland, Carlow JJ. Survivorship analysis of pedicle spinal instrumentation. Spine Phila Pa 1976. 1991;16:S422–7.

156. Dick JC, Bourgeault CA. Notch sensitivity of titanium alloy, commercially pure titanium, and stainless steel spinal implants. Spine Phila Pa 1976. 2001;26:1668–72.

157. Lindsey C, Deviren V, Xu Z, Yeh RF, Puttlitz CM. The effect of rod contouring on spinal construct fatigue strength. Spine Phila Pa 1976. 2006;31(15):1680–7.

158. M. Panjabi, G. Henderson, C. Abjornson, J. Yue. Multidirectional testing of one- and two-level ProDisc-L versus simulated fusions," Spine, vol. 32, no. 12, pp. 1311– 1319, 2007. Spine. 2007;32(12):1311–9.

159. B. Cakir, C. Carazzo, R. Schmidt, T. Mattes, H. Reichel, W. K¨afer. Adjacent segment mobility after rigid and semirigid instrumentation of the lumbar spine. Spine. 2009;34(12):1287–91.

160. Bhatia NN, Lee KH, Bui CNH, Luna M, Wahba GM, Lee TQ. Biomechanical evaluation of an expandable cage in single-segment posterior lumbar interbody fusion. Spine. 2012 Jan 15;37(2):E79–85.

161. Evans JH. Biomechanics of lumbar fusion. Clin Orthop. 1985 Mar;(193):38–46.

162. Wolff J. The Classic: On the Inner Architecture of Bones and its Importance for Bone Growth. Clin Orthop. 2010 Apr;468(4):1056–65.

163. Kowalski RJ, Ferrara LA, Benzel EC. Biomechanics of bone fusion. Neurosurg Focus. 2001;10(4):E2.

164. Sandhu HS, Turner S, Kabo JM, Kanim LE, Liu D, Nourparvar A, et al. Distractive properties of a threaded interbody fusion device. An in vivo model. Spine. 1996 May 15;21(10):1201–10.

165. Steffen T, Tsantrizos A, Aebi M. Effect of implant design and endplate preparation on the compressive strength of interbody fusion constructs. Spine. 2000 May 1;25(9):1077–84.

166. Oxland TR, Grant JP, Dvorak MF, Fisher CG. Effects of endplate removal on the structural properties of the lower lumbar vertebral bodies. Spine. 2003 Apr 15;28(8):771–7.

167. Cheng C-C, Ordway NR, Zhang X, Lu Y-M, Fang H, Fayyazi AH. Loss of cervical endplate integrity following minimal surface preparation. Spine. 2007 Aug 1;32(17):1852–5.

168. Harris BM, Hilibrand AS, Savas PE, Pellegrino A, Vaccaro AR, Siegler S, et al. Transforaminal lumbar interbody fusion: the effect of various instrumentation techniques on the flexibility of the lumbar spine. Spine. 2004 Feb 15;29(4):E65–70.

169. Moore J, Yoganandan N, Pintar FA, Lifshutz J, Maiman DJ. Tapered cages in anterior lumbar interbody fusion: biomechanics of segmental reactions. J Neurosurg Spine. 2006 Oct;5(4):330–5.

170. Kim S-M, Lim TJ, Paterno J, Park J, Kim DH. Biomechanical comparison: stability of lateral-approach anterior lumbar interbody fusion and lateral fixation compared with anterior-approach anterior lumbar interbody fusion and posterior fixation in the lower lumbar spine. J Neurosurg Spine. 2005 Jan;2(1):62–8.

171. Niemeyer TK, Koriller M, Claes L, Kettler A, Werner K, Wilke HJ. In vitro study of biomechanical behavior of anterior and transforaminal lumbar interbody instrumentation techniques. Neurosurgery. 2006 Dec;59(6):1271–6; discussion 1276–7.

172. Laws CJ, Coughlin DG, Lotz JC, Serhan HA, Hu SS. Direct lateral approach to lumbar fusion is a biomechanically equivalent alternative to the anterior approach: an in vitro study. Spine. 2012 May 1;37(10):819–25.

173. Chen H-H, Cheung H-H, Wang W-K, Li A, Li K-C. Biomechanical analysis of unilateral fixation with interbody cages. Spine. 2005 Feb 15;30(4):E92–6.

174. Chen S-H, Tai C-L, Lin C-Y, Hsieh P-H, Chen W-P. Biomechanical comparison of a new stand-alone anterior lumbar interbody fusion cage with established fixation techniques – a three-dimensional finite element analysis. BMC Musculoskelet Disord. 2008;9(1):88.

175. DiPaola CP, Molinari RW. Posterior lumbar interbody fusion. J Am Acad Orthop Surg. 2008 Mar;16(3):130–9.

176. Kumar N, Judith MR, Kumar A, Mishra V, Robert MC. Analysis of stress distribution in lumbar interbody fusion. Spine. 2005 Aug 1;30(15):1731–5.

177. Auerbach JD, Ballester CM, Hammond F, Carine ET, Balderston RA, Elliott DM. The effect of implant size and device keel on vertebral compression properties in lumbar total disc replacement. Spine J Off J North Am Spine Soc. 2010 Apr;10(4):333–40.

178. Le TV, Baaj AA, Dakwar E, Burkett CJ, Murray G, Smith DA, et al. Subsidence of polyetheretherketone intervertebral cages in minimally invasive lateral retroperitoneal transpsoas lumbar interbody fusion. Spine. 2012 Jun 15;37(14):1268–73.

179. Cole CD, McCall TD, Schmidt MH, Dailey AT. Comparison of low back fusion techniques: transforaminal lumbar interbody fusion (TLIF) or posterior lumbar interbody fusion (PLIF) approaches. Curr Rev Musculoskelet Med. 2009 Jun;2(2):118–26.

180. Weiner BK, Fraser RD. Spine update lumbar interbody cages. Spine. 1998 Mar 1;23(5):634–40.

181. Utzschneider S, Becker F, Grupp TM, Sievers B, Paulus A, Gottschalk O, et al. Inflammatory response against different carbon fiber-reinforced PEEK wear particles compared with UHMWPE in vivo. Acta Biomater. 2010 Nov;6(11):4296–304.

182. Morrison C, Macnair R, MacDonald C, Wykman A, Goldie I, Grant MH. In vitro biocompatibility testing of polymers for orthopaedic implants using cultured fibroblasts and osteoblasts. Biomaterials. 1995 Sep;16(13):987–92.

183. Wenz LM, Merritt K, Brown SA, Moet A, Steffee AD. In vitro biocompatibility of polyetheretherketone and polysulfone composites. J Biomed Mater Res. 1990 Feb;24(2):207–15.

184. Rousseau M-A, Lazennec J-Y, Saillant G. Circumferential arthrodesis using PEEK cages at the lumbar spine. J Spinal Disord Tech. 2007 Jun;20(4):278–81.

185. Youssef JA, McAfee PC, Patty CA, Raley E, DeBauche S, Shucosky E, et al. Minimally invasive surgery: lateral approach interbody fusion: results and review. Spine. 2010 Dec 15;35(26 Suppl):S302–11.

186. Boden SD, Schimandle JH, Hutton WC. An experimental lumbar intertransverse process spinal fusion model. Radiographic, histologic, and biomechanical healing characteristics. Spine. 1995 Feb 15;20(4):412–20.

187. Boden SD, Schimandle JH, Hutton WC, Chen MI. 1995 Volvo Award in basic sciences. The use of an osteoinductive growth factor for lumbar spinal fusion. Part I: Biology of spinal fusion. Spine. 1995 Dec 15;20(24):2626–32.

188. Ludwig SC, Boden SD. Osteoinductive bone graft substitutes for spinal fusion: a basic science summary. Orthop Clin North Am. 1999 Oct;30(4):635–45.

189. Xia X-P, Chen H-L, Cheng H-B. Prevalence of Adjacent Segment Degeneration After Spine Surgery: A Systematic Review and Meta-analysis. Spine. 2013 Apr;38(7):597–608.

190. Levin DA, Hale JJ, Bendo JA, others. Adjacent segment degeneration following spinal fusion for degenerative disc disease. Bull-Hosp Jt Dis N Y. 2007;65(1):29.

191. Wai EK, Santos ER, Morcom RA, Fraser RD. Magnetic resonance imaging 20 years after anterior lumbar interbody fusion. Spine. 31(17):1952–6.

192. Lee MJ, Dettori JR, Standaert CJ, Brodt ED, Chapman JR. The natural history of degeneration of the lumbar and cervical spines: a systematic review. Spine. 2012;37:S18–30.

193. Park P, Garton HJ, Gala VC, Hoff JT, McGillicuddy JE. Adjacent segment disease after lumbar or lumbosacral fusion: review of the literature. Spine. 2004;29(17):1938–44.

194. Yang JY, Lee J-K, Song H-S. The impact of adjacent segment degeneration on the clinical outcome after lumbar spinal fusion. Spine. 2008;33(5):503–7.

195. Okuda S, Iwasaki M, Miyauchi A, Aono H, Morita M, Yamamoto T. Risk factors for adjacent segment degeneration after PLIF. Spine. 2004;29(14):1535–40.

196. Yang SW, Langrana NA, Lee CK. Biomechanics of lumbosacral spinal fusion in combined compression-torsion loads. Spine. 1986;11:937-41. Spine. 1986;11:937–41.

197. Quinnell RC, Stockdale HR. Some experimental observations of the influence of a single lumbar floating fusion on the remaining lumbar spine. Spine. 1981;6:263–7.

198. Lee CK, Langrana. Lumbosacral spinal fusion. A biomechanical study. Spine. 1984;9:574–81.

199. Dmitriev AE, Cunningham BW, Hu N, Sell G, Vigna F, McAfee PC. Adjacent level intradiscal pressure and segmental kinematics following a cervical total disc arthroplasty: an in vitro human cadaveric model. Spine. 2005;30(10):1165–72.

200. Boden SDM, P R Davis, D O Dina, T S Mark, A S Wiesel, S. Abnormal magnetic-resonance scans of the cervical spine in asymptomatic subjects. A prospective investigation. J Bone Jt Surg. 1990 Sep 1;72(8):1178–84.

201. Ghiselli G, Wang JC, Hsu WK, Dawson EG. L5–S1 Segment Survivorship and Clinical Outcome Analysis After L4–L5 Isolated Fusion: Spine. 2003 Jun;28(12):1275–80.

202. Chen CS, Cheng CK, Liu CL. A biomechanical comparison of posterolateral fusion and posterior fusion in the lumbar spine. J Spinal Disord Tech. 2002;15:53–63.

203. Bastian L, Lange U, Knop C, Tusch G, Blauth M. Evaluation of the mobility of adjacent segments after posterior thoracolumbar fixation: a biomechanical study. Eur Spine J. 2001 Aug 1;10(4):295–300.

204. Umehara S, Zindeick MR, Patwardhan AG. The biomechanical effect of postoperative hypolordosis in instrumentated lumbar fusion on instrumented and adjacent spinal segments. Spine. 2000;25:1617–24.

205. Auerbach JD, Lonner BS, Errico TJ, Freeman A, Goerke D, Beaubien BP. Quantification of Intradiscal Pressures Below Thoracolumbar Spinal Fusion Constructs: Is There Evidence to Support “Saving a Level?.” Spine. 2012 Mar;37(5):359–66.

206. Cunningham BW, Kotani Y, McNulty PS. The effect of spinal destabilization and instrumentation on lumbar intradiscal pressure:an in vitro biomechanical analysis. Spine. 1997;22:2655–63.

207. Kee-yong Ha, Jong-Min Son, Jin-Hyung Im, In-Soo Oh. Risk factors for adjacent segment degeneration after surgical correction of degenerative lumbar scoliosis. Indian J Orthop. 2013;Vol47(Issue 4).

208. Chen B-L, Wei F-X, Ueyama K, Xie D-H, Sannohe A, Liu S-Y. Adjacent segment degeneration after single-segment PLIF: the risk factor for degeneration and its impact on clinical outcomes. Eur Spine J. 2011 Nov;20(11):1946–50.

209. Cho KS, Kang SG, Yoo DS. Risk factors and surgical treatment for symptomatic adjacent segment degeneration after lumbar spine fusion. J Korean Neurosurg Soc. 2009;46:425–30.

210. Lawrence BD, Wang J, Arnold PM, Hermsmeyer J, Norvell DC, Brodke DS. Predicting the risk of adjacent segment pathology after lumbar fusion: a systematic review. Spine. 2012;37:S123–32.

211. Okuda S, Oda T, Miyauchi A. Lamina horizontalization and facet tropism as the risk factors for adjacent segment degeneration after PLIF. Spine. 2008;33:2754–8.

212. Choma TJ, Schuster JM, Norvell DC, Dettori JR, Chutkan NB. Fusion Versus Nonoperative Management for Chronic Low Back Pain: Do Comorbid Diseases or General Health Factors Affect Outcome? Spine. 2011 Oct;36:S87–95.

213. Chow DHK, Luk KDK, Evans JH, Leong JCY. Effects of Short Anterior Lumbar Interbody Fusion on Biomechanics of Neighboring Unfused Segments. Spine [Internet]. 1996;21(5). Available from: http://journals.lww.com/spinejournal/Fulltext/1996/03010/Effects_of_Short_Anterior_Lumbar_Interbody_Fusion.4.aspx

214. Nagata H, Schendel MJ, Transfeldt EE, Lewis JL. The Effects of Immobilization of Long Segments of the Spine on the Adjacent and Distal Facet Force and Lumbosacral Motion. Spine [Internet]. 1993;18(16). Available from: http://journals.lww.com/spinejournal/Fulltext/1993/12000/The_Effects_of_Immobilization_of_Long_Segments_of.17.aspx

215. Kumar M, Baklanov A, Chopin D. Correlation between sagittal plane changes and adjacent segment degeneration following lumbar spine fusion. Eur Spine J. 2001 Aug;10(4):314–9.

216. Park JY, Cho YE, Kuh SU, Cho JH, Chin DK, Jin BH, et al. New prognostic factors for adjacent-segment degeneration after one-stage 360° fixation for spondylolytic spondylolisthesis: special reference to the usefulness of pelvic incidence angle. J Neurosurg Spine. 2007 Aug 1;7(2):139–44.

217. Hioki A, Miyamoto K, Kodama H, Hosoe H, Nishimoto H, Sakaeda H, et al. Two-level posterior lumbar interbody fusion for degenerative disc disease: improved clinical outcome with restoration of lumbar lordosis. Spine J. 2005 Nov;5(6):600–7.

218. Chen WJ, Lai PL, Tai CL, Chen LH, Niu CC. The effect of sagittal alignment on adjacent joint mobility after lumbar instrumentation—a biomechanical study of lumbar vertebrae in a porcine model. Clin Biomech. 2004 Oct;19(8):763–8.

219. Nagaosa Y, Kikuchi S, Hasue M, Sato S. Pathoanatomic Mechanisms of Degenerative Spondylolisthesis: A Radiographic Study. Spine [Internet]. 1998;23(13). Available from: http://journals.lww.com/spinejournal/Fulltext/1998/07010/Pathoanatomic_Mechanisms_of_Degenerative.4.aspx

220. Nassr A, Lee JY, Bashir RS, Rihn JA, Eck JC, Kang JD, et al. Does Incorrect Level Needle Localization During Anterior Cervical Discectomy and Fusion Lead to Accelerated Disc Degeneration? Spine [Internet]. 2009;34(2). Available from: http://journals.lww.com/spinejournal/Fulltext/2009/01150/Does_Incorrect_Level_Needle_Localization_During.14.aspx

221. Park J-BC, Yong-Sun Riew, K. Daniel. Development of Adjacent-Level Ossification in Patients with an Anterior Cervical Plate. J Bone Jt Surg. 2005 Mar 1;87(3):558–63.

222. Kasliwal MK, Shaffrey CI, Lenke LG, Dettori JR, Ely CG, Smith JS. Frequency, Risk Factors, and Treatment of Distal Adjacent Segment Pathology After Long Thoracolumbar Fusion: A Systematic Review. Spine. 2012 Oct;37:S165–79.

223. Cochran T, Irstam L, Nachemson A. Long-term anatomic and functional changes in patients with adolescent idiopathic scoliosis treated by Harrington rod fusion. Spine. 1983;8:576–84.

224. Whitecloud TS, Davis JM, Olive PM. Operative treatment of the degenerated segment adjacent to a lumbar fusion. Spine. 1994;19:531–6.

225. Kawakami M, Tamaki T, Ando M. Lumbar sagittal balance influences the clinical outcome after decompression and posterolateral spinal fusion for degenerative lumbar spondylolisthesis. Spine. 2002;27(1):59–64.

226. Lagrone MO, Bradford DS, Moe JH. Treatment of symptomatic flatback after spinal fusion. J Bone Jt Surg Am. 1988 Apr;70(4):569–80.

227. Hilibrand AS, Carlson GD, Palumbo MA, Jones PK, Bohlman HH. Radiculopathy and Myelopathy at Segments Adjacent to the Site of a Previous Anterior Cervical Arthrodesis*. J Bone Jt Surg. 1999;81(4):519–28.

228. Ekman P, Mo¨ller H, Shalabi A. A prospective randomised study on the long-term effect of lumbar fusion on adjacent disc degeneration. Eur Spine J. 2009;18:1175–86.

229. Lorenz M, Zindrick M, Schwaegler P. A comparison of single-level fusions with and without hardware. Spine. 1991;16:S455–8.

230. Zdeblick T. A prospective randomized study of lumbar fusion: preliminary results. Spine. 1993;18:983–91.

231. Pfirrmann CW, Metzdorf A, Zanetti M, Hodler J, Boos N. Magnetic resonance classification of lumbar intervertebral disc degeneration. Spine. 2001;26(17):1873–8.

232. Pope MH, Wilder DG, Matteri RE, Frymoyer JW. Experimental measurements of vertebral motion under load. Orthop Clin North Am. 1977;8:155–67.

233. Kim KH, Park JY, Chin DK. Fusion Criteria for Posterior Lumbar Interbody Fusion with Intervertebral Cages : The Significance of Traction Spur. J Korean Neurosurg Soc. 2009 Oct;46(4):328–32.

234. Fujiwara A, Tamai K, Yamato M, An HS, Yoshida H, Saotome K, et al. The relationship between facet joint osteoarthritis and disc degeneration of the lumbar spine: an MRI study. Eur Spine J. 1999;8(5):396–401.

235. Carlsson AM. Assessment of chronic pain. I. Aspects of the reliability and validity of the visual analogue scale. Pain. 1983 May;16(1):87–101.

236. Bijur PE, Silver W, Gallagher EJ. Reliability of the Visual Analog Scale for Measurement of Acute Pain. Acad Emerg Med. 2001 Dec 1;8(12):1153–7.

237. DeLoach LJ, Higgins MS, Caplan AB, Stiff JL. The visual analog scale in the immediate postoperative period: intrasubject variability and correlation with a numeric scale. Anesth Analg. 1998;86(1):102–6.

238. Greenough CG, Fraser RD. Assessment of outcome in patients with low back pain. Spine. 1992;17:36–41.

239. Costanzo G, Cellocco P, Francesco AD, Rossi C. The role of JOA score as an indication for surgical or conservative treatment of symptomatic degenerative lumbar spinal stenosis. J Orthop Traumatol. 2005 Oct 1;6(3):150–3.

240. Hirabayashi K, Watanabe K, Wakano K. Expansive opendoor laminoplasty for cervical spinal stenotic myelopathy. Spine. 1983;8:693–9.

ANNEXURES

ANNEXURE-1

INSTITUTIONAL REVIEW BOARD (IRB)
CHRISTIAN MEDICAL COLLEGE
VELLORE 632 002, INDIA

Dr. B J Prashantham, M.A, M. A., Dr. Min (Clinical)
Director, Christian Counselling Centre
Chairperson, Ethics Committee

Dr. Alfred Job Daniel, D Ortho MS Ortho DNB Ortho
Chairperson, Research Committee & Principal

Dr. Nihal Thomas
MD,MNAMS, DNB(Endo), FRACP(Endo), FRCP(Edin)
Secretary, Ethics Committee, IRB
Additional Vice Principal (Research)

April 8, 2013

Dr. Jeremy Bliss
PG Registrar
Department of Orthopaedics
Christian Medical College
Vellore 632 002

Sub: **FLUID Research grant project NEW PROPOSAL:**
A Comparative Study: Incidence of Adjacent Segment Degeneration following single level Instrumental fusion and single level diskectomy.
Dr. Jeremy Bliss, PG, Orthopaedics, Dr. Venkatesh, Orthopaedics.

Ref: IRB Min. No. 7979 dated 08.09.2012

Dear Dr. Jeremy Bliss,

The Institutional Review Board (Blue, Research and Ethics Committee) of the Christian Medical College, Vellore, reviewed and discussed your project entitled "A Comparative Study: Incidence of Adjacent Segment Degeneration following single level Instrumental fusion and single level diskectomy. " on September 8, 2012.

The Committees reviewed the following documents:

1. Format for application to IRB submission
2. Information Sheet and Informed Consent Form
3. Patient Information Sheet
4. Proforma
5. Cv of Dr. Jeremy Bliss
6. A CD containing documents 1 - 4

TEL : 0416 - 2284294, 2284202 FAX : 0416 - 2262788, 2284481 E-mail : research@cmcvellore.ac.in

INSTITUTIONAL REVIEW BOARD (IRB)
CHRISTIAN MEDICAL COLLEGE
VELLORE 632 002, INDIA

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Dr. Nihal Thomas
MD,MNAMS, DNB(Endo), FRACP(Endo), FRCP(Edin)
Secretary, Ethics Committee, IRB
Additional Vice Principal (Research)

The following Institutional Review Board (Research & Ethics Committee) members were present at the meeting held on September 8, 2012 in the CREST/SACN Conference Room, Christian Medical College, Bagayam, Vellore 632002.

Name	Qualification	Designation	Other Affiliations
Mr. Sampath	BSc, BL	Advocate	External Legal Expert
Mrs. Ellen Ebenezer Benjamin	M.Sc. (Nursing), Ph.D.	Professor, Maternity Nursing, CMC.	Internal, Nurse
Mr. T.S. Ravikumar	MSC	Professor, Medical Surgical Nursing, CMC	Internal
Mr. Harikrishnan	BL	Lawyer, Vellore	External, Legal Expert
Mr. Joseph Devaraj	BSc, BD	Chaplain, CMC	Internal, Social Scientist
Dr. Priya Abraham	MBBS, MD, PhD	Professor, Virology, CMC	Internal, Clinician
Dr. Bobby John	MBBS, MD, DM, PhD, MAMS	Professor, Cardiology, CMC.	Internal, Clinician
Dr. Anil Kuruvilla	MBBS, MD, DCH	Professor, Neonatology, CMC.	Internal, Clinician
Dr. Simon Rajaratnam	MBBS, MD, DNB (Endo), MNAMS (Endo), PhD (Endo), FRACP	Professor, Endocrinology, CMC	Internal, Clinician
Dr. Mathew Joseph	MBBS, MCH	Professor, Neurosurgery, CMC	Internal, Clinician
Dr. Benjamin Perakath	MBBS, MS, FRCS	Professor, Surgery (Colorectal), CMC.	Internal, Clinician
Dr. Paul Ravindran	PhD, Dip RP, FCCPM	Professor, Radiotherapy, CMC	Internal
Dr. Sujith Chandy	MBBS, MD	Professor, Pharmacology & Clinical Pharmacology, CMC.	Internal, Pharmacologist
Dr. Denny Fleming	BSc (Hons), PhD	Honorary Professor, Clinical Pharmacology, CMC.	Internal, Pharmacologist

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VELLORE 632 002, INDIA

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MD,MNAMS, DNB(Endo), FRACP(Endo), FRCP(Edin)
Secretary, Ethics Committee, IRB
Additional Vice Principal (Research)

Dr. Ranjith K Moorthy	MBBS MCh	Professor, Neurological Sciences, CMC	Internal, Clinician
Dr. Nihal Thomas	MD MNAMS DNB(Endo) FRACP(Endo) FRCP(Edin)	Secretary IRB (EC)& Dy. Chairperson (IRB),	Internal, Clinician

We approve the project to be conducted as presented.

The Institutional Ethics Committee expects to be informed about the progress of the project, any serious adverse events occurring in the course of the project, any changes in the protocol and the patient information/informed consent. And on completion of the study you are expected to submit a copy of the final report.

Yours sincerely

Dr. Nihal Thomas
Secretary (Ethics Committee)
Institutional Review Board

Dr Nihal Thomas
MBBS MD MNAMS DNB (Endo) FRACP(Endo) FRCP(Edin)
Secretary (Ethics Committee)
Institutional Review Board

CC: Dr. Venkatesh, Department of Orthopaedics, CMC

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ANNEXURE-2

PATIENT INFORMATION SHEET IN ENGLISH

PATIENT INFORMATION SHEET

This is a Research taking place in the Spinal Disorders Surgery Unit of the Department of Orthopaedics in CMC, Vellore. It is being conducted by Dr. Jeremy Bliss under the guidance of Dr. Venkatesh. The purpose of this study is to call back all patients - a total of more than 1500 patients, who underwent two types of surgeries i.e., Single Level Lumbar Fusion and Single Level Discectomy during the years 2006 to 2010 and evaluate them with X-ray's, MRI & clinically to find out the outcome of the surgeries they had undergone, and make them aware of the same and advice for future plan of treatment if needed or else advice regarding life style modifications. For all this the patient may have to stay in Vellore for a minimum of 2 days. The possible risks involved are the exposure to radiation while taking X-Rays and MRI. The patient's details and concerned medical records will be kept confidential and will be accessed by only the study team. The responsibility of the patient while participating in the study is to adhere to the advice given and follow all the physiotherapy protocols taught. The patient can willingly take part in the study and can also decide to withdraw from participating at his or her own will.

ANNEXURE-3

PATIENT INFORMATION SHEET IN HINDI

रोगी सूचना पत्र

यह अनुसंधान डा० जेरेमी डेविस द्वारा डा० वेंकटेश के मार्गदर्शन में सी० एम सी० अस्पताल (CMC HOSPITAL) के अस्थि शल्य विभाग की रीढ़ की हड्डी में विकार यूनिट (SPINAL DISORDER SURGERY UNIT) के अधीन किया जा रहा है। इस अनुसंधान के अंतर्गत करीब 1500 रोगियों का, जिनका C.M.C अस्पताल में 2006 - 2009 के बीच या तो रीढ़ की हड्डी के एक स्तर का फ्यूजन (Fusion) या डिस्केक्टमी (discectomy) किया गया है, उनका चिकित्सिय जाँच एक्सरे और MRI. के साथ किया जाएगा। इस जाँच का उद्देश्य सर्जरी के परिणाम को जानना तथा यह पता करना है कि भविष्य में कोई उपचार की जरूरत है कि नहीं। इसका उद्देश्य जीवन शैली में संशोधन के सलाह के बारे में पता करना भी है। इस अध्ययन के लिए रोगी को वेल्लूर में कम से कम दो दिनों तक ठहरना पड़ सकता है।

इस अध्ययन में शामिल होने से रोगी को X-ray (विकिरण) के संपर्क में आने के अलावा कोई अतिरिक्त जोखिम नहीं है। इसका शरीर पर प्रभाव न्यूनतम है। इस अध्ययन से उत्पन्न मरीज के बारे में जानकारी और संबंधित चिकित्सा अभिलेखों को गोपनीय रखा जाएगा और इसका उपयोग सिर्फ अध्ययन दल के सदस्यों द्वारा किया जाएगा। इस अध्ययन में मरीज से यह अपेक्षा की जाती है कि वह डा० द्वारा बताए सलाहों का पालन करे। मरीज स्वेच्छा से इस अध्ययन में भाग ले सकता है और किसी भी समय अपना नाम वापस ले सकता है।

ANNEXURE-4

PATIENT INFORMATION SHEET IN TAMIL

நோயாளி தகவல் தாள்

கிரிஸ்துவ மருத்துவ கல்லூரி மருத்துவமனை, வேலூரில் உள்ள எலும்பு துரையின் முதுகுத்தண்டு நோய்கள் அறுவை சிகிச்சை பிரிவில் நடக்கும் ஒரு ஆராய்ச்சி இது. இதனை டாக்டர் வெங்கடேஷ் வழிகாட்டுதலின் கீழ் டாக்டர் ஜெர்மி ப்ளிஸ் நடத்துகிறார்.

இந்த ஆய்வின் நோக்கம்: ஆண்டுகள் 2006 முதல் 2010 வரை நடந்த இரண்டு வகையான சிகிச்சைகள், அதாவது ஒற்றை நிலை கீழ்முதுகு Fusion மற்றும் ஒற்றை நிலை Discectomy ஆகிய சிகிச்சைகளை மேற்கொண்ட சுமார் 1500 நோயாளிகளை மீண்டும் அழைத்து, X-கதிர், MRI, கேள்விக்கணைகள் மற்றும் மருத்துவ பரிசோதனை மூலம் அவர்களை மதிப்பீடு செய்வதுதான். அவர்கள் கடந்து வந்த அறுவை சிகிச்சையின் விளைவை பற்றி அவர்களுக்கு தெளிவுபடுத்தப்படும். எதிர்கால சிகிச்சை தேவைப்பட்டால் அதனை பற்றிய ஆலோசனையும் வழங்கப்படும் இல்லையெனில் வாழ்க்கை பாணி திருத்தங்கள் மற்றும் உடற்பயிற்சி பற்றிய ஆலோசனைகள் வழங்கப்படும்.

இந்த நோக்கத்திற்காக நோயாளி குறைந்தது 2 நாட்கள் வேலூரில் தங்க வேண்டும், போக்குவரத்து மற்றும் தங்கும் செலவுகளை நோயாளி ஏற்க வேண்டும். ஆய்வில் X-கதிர்கள் எடுக்கும் போது கதிர்வீச்சின் திங்குர்க்கு ஆளாக்கப்படும் அபாயம் உள்ளது. நோயாளியின் விவரங்கள் மற்றும் சம்பந்தப்பட்ட மருத்துவ பதிவுகள் பாதுகாப்பாக ஆய்வு குழுவால் பராமரிக்கப்படும்.

ஆய்வில் பங்கேற்கும் நோயாளியின் பொறுப்பு: ஆய்வின் போது கொடுக்கப்பட்ட ஆலோசனைகளையும் கற்ற அனைத்து பிசியோதெரபி நெறிமுறைகளையும் பின்பற்ற வேண்டும். நோயாளி அவரது சொந்த விருப்பத்துடன் ஆய்வில் பங்கேற்க முடியும், மேலும் அவரது சொந்த விருப்பத்தின் பேரில் ஆய்விலுருந்து விலகிகொள்ளவும் முடியும்.

விபரங்கள்:

தொலைபேசி எண்: 04162282731

முகவரி:

முதுகுத்தண்டு நோய்கள் அறுவை சிகிச்சை பிரிவு,
பால் பிராண்ட் பில்டிங்,
CMC மருத்துவமனை வளாகம்,
வேலூர்-632004

ANNEXURE-5

PATIENT INFORMATION SHEET IN TELUGU

ఇది క్రిస్టియన్ మెడికల్ కాలేజ్ వేలూర్ లోని వెన్నెముక శస్త్ర చికిత్స, అర్తోపేడిక్స్ విభాగం లో జరుగుతున్న ఒక పరిశోదన. ఇది డాక్టర్ వెంకటేష్ ఆధ్వర్యం లో డాక్టర్ జెరిమీ బ్లిస్ చేస్తున్నారు. 2006 నుండి 2010 వరకు ఒక్క లంబార్ వెన్ను స్థాయిలో ఫ్యూషన్ లేదా డిస్కెక్టమీ అనబడే శస్త్ర చికిత్స చెయ్య బడిన రోగులలో నుండి 1500 లేదా అంతకన్నా ఎక్కువ మందిని పిలిపించి వారి లోని శాస్త్ర చికిత్స ఫలితాన్ని X రే, యం ఆర్ ఐ, మరియు వైద్య పరంగా విశ్లేషించి ఫలితాన్ని రోగులకు తెలియ పరచి, చికిత్స యొక్క భవిష్యత్తు ప్రణాళికను, అవసరమైతే జీవన శైలి లో మార్పులను గురించి సలహా ఇవ్వబడుతుంది. దీనంతటి కొరకు రోగి వేలూర్ లో కనీసం 2 రోజులు బస చేయవలెను. X రే మరియు యం ఆర్ ఐ వలన రేడియేషన్ యొక్క ప్రమాదం ఉండే అవకాశముంది. రోగి యొక్క వివరాలు, సంబంధిత వైద్య నివేదికలు గోప్యంగా ఉంచబడతాయి మరియు అధ్యయన బృందం మాత్రమే వీటిని పరిశీలిస్తారు. బోధించబడిన సలహాను పాటించడం మరియు పిసియోతెరపీ లో నేర్పబడినవి తప్పకుండా చేయుట అనేది ఈ అధ్యయనం లో పాల్గొన్న సమయం లో రోగి యొక్క బాధ్యత.

ANNEXURE-6

PATIENT INFORMATION SHEET IN BENGALI

রোগীর জন্য তথ্যপত্র

এটি একটি এমন রিসার্চ বা গবেষণামূলক পরীক্ষা, যা ভেলোর সিএমসি (CMC) হাসপাতালের মেরুদন্ড রোগ সম্পর্কিত (Spinal disorders), Orthopaedics বিভাগের অর্থোপেডিক ইউনিটে অনুষ্ঠিত হবে। এই পরীক্ষা Dr. Venkatesh -এর অধীনে, Dr. Jeremy Bliss দ্বারা পরিচালিত হচ্ছে। এই গবেষণার উদ্দেশ্য, সেই সকল প্রায় ১৫০০ রোগীকে পুনরায় আহ্বান করা, যারা নাকি ২০০৬ থেকে ২০১০ সালের মধ্যে দুই প্রকার অর্থোপেডিক চিকিৎসায় অংশ নিয়েছেন, যেমন ১) Single Level Lumber Fusion ও ২) Single Level Discetomy, তাঁদের এক্সরে, এমআরআই এবং অন্যান্য চিকিৎসার মূল্যায়ণ করা হবে ও যে অস্ত্রোপচার তাঁদের হয়েছে, তার ফলাফল কি সেই তথ্য তাদের জানানো ও ভবিষ্যতে কি প্রকার চিকিৎসা হবে সেই পরিকল্পনা সম্পর্কে যদি জীবনশৈলী পরিবর্তনের প্রয়োজন, তার পরামর্শ দান। এই সকলের জন্য রোগীদের হয়তো কমপক্ষে ২ দিন ভেলোর-এ থাকতে হতে পারে। যখন এক্সরে ও এমআরআই নেওয়া হবে তখন Radiation বা বিকিরণের ঝুঁকি থাকবে। রোগীর বিবরণ ও রোগ সম্পর্কিত তথ্য গোপন রাখা হবে। কেবল গবেষণা / অধ্যয়নকারী চিকিৎসক দল তা প্রয়োজনে ব্যবহার করবেন । গবেষণায় অংশগ্রহণ কালে রোগী অবশ্যই ফিজিওথেরাপী প্রোটোকল সম্পর্কিত পরামর্শ মানতে দৃঢ় সংকল্প থাকবেন। রোগী স্বেচ্ছায় গবেষণায় অংশ নিতে বা স্বেচ্ছায় নিজেকে প্রত্যাহার করার সিদ্ধান্ত নিতে পারবেন।

ANNEXURE-7

PATIENT INFORMED CONSENT SHEET IN ENGLISH

INFORMED CONSENT FORM

Patient's Name:
Hospital Number:

(i) I confirm that I have read and understood the information sheet for the above study and have had the opportunity to ask questions. [ ]

(ii) I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. [ ]

(iii) I understand that the Ethics Committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published. [ ]

(iv) I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s) [ ]

(v) I agree to take part in the above study. [ ]

Signatory's Name: _____ Date: _____/_____/_____	Signature (or Thumb impression) of the Subject/Legally Acceptable Representative:
Study Investigator's Name: _____ Date: _____/_____/_____	Signature of the Investigator:
Name of the Witness: _____ Date:_____/_____/_____	Signature of the Witness:

ANNEXURE-8

PATIENT INFORMED CONSENT SHEET IN HINDI

रोगी सूचित स्वीकृति पत्र

परियोजना का शीर्षक -
अन्वेषक -

इस सूचना पत्र के विषय को मैंने सावधानीपूर्वक पढ़ लिया है / मुझे मेरी भाषा में विस्तार से समझा दिया गया है जो मुझे समझ में आती है और मैंने पूरे विषय को अच्छी तरह समझ लिया है। मैं पुष्टि करता हूँ कि मुझे प्रश्न पूछने का अवसर दिया गया है। मैं निम्नलिखित को समझता/समझती हूँ।

1). अध्ययन का प्रकार और प्रयोजन तथा अध्ययन के अन्य संगत विवरण मुझे विस्तार से समझा दिए गए हैं।

2) मुझे बताया गया है कि मेरी भागीदारी स्वेच्छानुसार है और मैं कोई कारण बताए बिना किसी भी समय इस अध्ययन से अपना नाम वापस ले सकता हूँ। ऐसा करने पर मेरी चिकित्सा देखभाल या कानूनी अधिकारों पर कोई प्रभाव नहीं पड़ेगा।

3). मुझे पता है कि इस अनुसंधान में मेरी भागीदारी के बारे में जमा की गई जानकारी और नमूनों को CMC के जिम्मेदार व्यक्तियों (जो कि आचार समिति और विनियामक प्राधिकारणों से हैं) द्वारा देखी जाएगी और इसका उपयोग अनुसंधान के विषय में किया जाएगा। मैं इसके लिए अपनी अनुमति देता हूँ। हालांकि मैं समझता हूँ कि मेरी पहचान को प्रकाशित जानकारी में गुप्त रखा जाएगा और किसी तीसरे पक्ष के सामने इसे उजागर नहीं किया जाएगा।

4) इस अनुसंधान के द्वारा जो भी नमूने और निष्कर्ष निकलते हैं, उनका उपयोग अगर सिर्फ वैज्ञानिक अध्ययन के संबंध में किया जाता है तो इसमें मुझे कोई आपत्ति नहीं है।

मैं उपरोक्त अध्ययन में भाग लेने के लिए सहमत हूँ।

हस्ताक्षर
नाम
तिथि

गवाह के हस्ताक्षर
गवाह के नाम
तिथि

अन्वेषक का हस्ताक्षर
जाँचकर्ता का नाम
तिथि

ANNEXURE-9

PATIENT INFORMED CONSENT SHEET IN TAMIL

தகவல் ஏற்றுக்கொண்டாக படிவம்

நோயாளியின் பெயர்:
மருத்துவமனை எண்:

(I) மேலே உள்ள ஆய்வு தகவல் தாளை நான் படித்து புரிந்து கொண்டேன் என்றும் கேள்விகள் கேட்க வாய்ப்பு கிடைத்தது என்று உறுதி செய்கிறேன்.[ ]

(II) இந்த ஆய்வில் பங்கேற்பது என் விருப்பம் என்றும், நான் எந்த நேரத்திலும் எந்த காரணமும் கொடுக்காமல், என் மருத்துவ தேவைகள் மற்றும் சட்ட உரிமைகள் பாதிக்காமல் விலகிக்கொள்ள முடியும் என்று புரிந்துகொள்கிறேன்.[ ]

(III) நெறிமுறைகள் குழு மற்றும் கட்டுப்பாட்டு அதிகாரிகள் தற்போதைய ஆய்விற்க்கும் மேலும் எதிர்கால ஆராய்ச்சிகள் தொடர்பாக என் மருத்துவ பதிவுகளை பார்க்க என் அனுமதி தேவையில்லை என்று புரிந்துகொள்கிறேன். நான் இந்த அணுகலுக்கு ஒப்புக்கொள்கிறேன். எனினும், என் அடையாளம் மூன்றாவது நபர்களுக்கு வெளியிடப்படாது என்பதை புரிந்துகொண்டேன்.[ ]

(IV) இந்த ஆய்வில் எழும் எந்த முடிவுகளை நான் அறிவியல் நோக்கத்திற்காக பயன்படுத்த எனக்கு தடை இல்லை.[ ]

(V) இந்த ஆய்வில் பங்கேற்க நான் ஏற்கிறேன்.[ ]

பெயர்:
தேதி:
கையொப்பம்/அல்லது கைநாட்டு:

விசாரணை செய்பவரின் பெயர்:
தேதி:
கையொப்பம்:

சாட்சியின் பெயர்:
தேதி:
கையொப்பம்:

ANNEXURE-10

PATIENT INFORMED CONSENT SHEET IN TELUGU

ఒకే స్థాయిలో నడుము యాంత్రిక కలయిక మరియు ఒకే స్థాయిలో డిస్క్రెక్తమి తరువాత ప్రక్కన విభాగంలో తీవ్ర సంభవించుట - ఒక తులనాత్మక అధ్యయనం

సమ్మతి పత్రం

రోగి యొక్క పేరు

హాస్పిటల్ సంఖ్య

(i) నేను పైన అధ్యయనం కోసం సమాచారం పేజీ చదివి అర్థం చేసుకున్నాను మరియు ప్రశ్నించేందుకు అవకాశం కలిగింది అని నిర్ధారిస్తున్నాను.

(ii) ఈ అధ్యయనం లో నేను పాలుపొందుట నా స్వచ్ఛంద నిర్ణయం అనియు, ఏ సమయం లో అయిన, వికారణం లేకుండా అయిన నేను వెనుతిరుగుట వలన నాకు వైద్య మరియు చట్ట సంబంధంగా ఎటువంటి ఇబ్బంది ఉండదు అని నేను అర్థం చేసుకున్నాను.

(iii) ఎథిక్స్ కమిటీ మరియు నియంత్రణ అధికారులు ఈ అధ్యయనం కొరకు మరియు భవిష్యత్తులో నేరే పరిశోధనల కొరకు, ఒక వేళ నేను ఈ అధ్యయనం నుండి వెనుదిరిగినప్పటికి నా ఆరోగ్య రికార్డులను పరిశోధించుటకు నా అనుమతి అవసరం లేదని నేను అర్థం చేసుకున్నాను. ఈ ప్రాజెక్ట్ కి నేను అంగీకరిస్తున్నాను. అయినప్పటికి, నా గుర్తింపు మూడవ పార్టీకి బయలుపరచబడదు అనియు ముద్రింపబడదు అనియు నేను అర్థం చేస్కున్నాను.

(iv) ఈ అధ్యయనం ద్వారా ఉత్పన్నమయ్యే ఏ డేటా లేదా ఫలితాలు శాస్త్రీయ ప్రయోజనం కోసం ఉపయోగించుటకు నేను అభ్యంతరం అని ఒప్పుకుంటున్నాను.

(v) నేను పై అధ్యయనం పాల్గొనడానికి అంగీకరిస్తున్నాను

సంతకం లేదా వేలు ముద్ర పేరు మరియు సంతకం

తేది తేది

అధ్యయన పరిశోధకుల పేరు మరియు సంతకం

తేది

ANNEXURE-11
PATIENT INFORMED CONSENT SHEET IN BENGALI

সকল তথ্য জেনে ও বুঝে অনুমতি প্রদান পত্র

রোগীর নাম - _____

হাসপাতাল সংখ্যা- _____

১। আমি স্বীকার করি যে, উপরোক্ত অধ্যয়নের বিষয়বস্তু, আমি পড়েছি ও বুঝেছি এবং প্রশ্ন করার সুযোগ পেয়েছি।

২।- আমি বুঝেছি যে এই গবেষণায় আমি স্বেচ্ছায় অংশগ্রহণ করছি। আমি কোন কারণ না দেখিয়ে যে কোন সময় গবেষণা থেকে সরে আসতে পারি। এবং তার ফলে কোন ভাবেই আমার চিকিৎসায় প্রভাব পড়বে না অথবা আইনসঙ্গত অধিকার খর্ব হবে না।

৩। — আমি এটাও বুঝতে পেরেছি যে, এথিক্স কমিটি এবং নিয়ন্ত্রক কর্তৃপক্ষ আমার বর্তমান ও আগামী দিনের পরীক্ষামূলক হেল্থ রেকর্ড, আমার অনুমতি ছাড়াই দেখতে পাবেন, এমন কি আমি যদি ওই পরীক্ষা থেকে নিজেকে প্রত্যাহার করি, তবুও। যাই হোক, আমি বুঝেছি যে ওই তথ্য যদি কোন তৃতীয় পক্ষ বা পত্রিকায় প্রকাশিত হয়, তবে আমার পরিচয় গোপন রাখা হবে।

৪। — যদি কেবলমাত্র বিজ্ঞানভিত্তিক উদ্দেশ্যে ওই পরীক্ষার ফল বা তথ্য ব্যবহার হয় তবে আমি কখনই আপত্তি জানাবো না বলে সম্মতি দিলাম।

৫। — আমি উপরোক্ত গবেষণায় অংশ নিতে রাজি হলাম।

স্বাক্ষরকারী এর নাম _____ তারিখ - _____	আইনত গ্রহণযোগ্য প্রতিনিধির স্বাক্ষর (বা বুড়ো আঙুলের ছাপ)
অধ্যয়ণ তদন্তকারী-এর নাম _____ তারিখ - _____	তদন্তকারী স্বাক্ষর
সাক্ষীর নাম _____ তারিখ - _____	সাক্ষীর স্বাক্ষর

ANNEXURE-12

INVESTIGATORS BROCHURE

INVESTIGATORS BROCHURE

Patients Name									
Hospital Number									
Phone Number							**Address Updated**		

Diagnosis						
Surgery Done						
Date of Surgery						
Date of Follow-up				***Duration***	*Year/s*	*Months*

Height		*Cm*						
Weight	**Pre-op**		*Kg*		**Follow-up**		*Kg*	
Smoking		YES	NO	*Duration*				
Tobacco chewing		YES	NO	*Duration*				
Alcohol		YES	NO	*Duration*				
Past History of		Trauma	Cough	*Fever*	*Weight Loss*			
Comorbidities							*Duration*	

Pre-Operative Occupation					
Disability Period				*Duration*	
Post-Operative Occupation	SAME	MODIFIED	DIFFERENT		

Pre-op Symptoms				*Duration*	
Post-op Relief of Symptoms	COMPLETE		INCOMPLETE	RESIDUAL	
Physiotherapy	REGULAR	IRREGULAR	CONTINOUS	*Duration*	
Corset/Aid Used				*Duration*	
New Symptoms	YES	NO		*Duration*	
Post-op Infection	YES	NO			
Re-Surgery	YES	NO			

SCORES	**Pre-Op**	**Follow-up**	**NOTES:**			
VAS						
ODI						
JOA			**CHECKLIST**			
H %			*PRP XRAY*	*POP XRAY*	*PRP MRI*	*POP MRI*

NO	NAME	H.NUM	SUBDIAGNOSIS	AGE	SEX	BMI	COM	OCC	SMOKE	FU	DX	SX	OPS	PY	DOC	PGR1	PGR2	PGR3	PGR4	PGR5	PGO1	PGO2	PGO3	PGO	PGO5	CPL	CPR	ASL	ASR	CDL	CDR	CPL	CPR	ASL	ASR	CDL	CDR	DHPRP	DHPOP	DHFU	FUS	VASR	VASO	ODIR	ODIO	JOAR	JOAO	HRR
1	SWAPAN KUMAR	584214D		29	1	99	3	1	FALSE	56	1	1	5	99	4	1	1	1	1	3	1	1	1	1	4	2	2	2	2	99	99	2	2	3	3	99	99	12		11.88		10	8	60	88	12	12	11
2	MANI MEGALAI M.	707915C		55	2	99	1	3	FALSE	44	1	1	4	99	1	3	3	2	4	3	4	4	3	5	3	2	2	2	2	1	2	2	2	2	2	2	2	4.3		3.25		10	4	72	24	17	22	41
3	BABU	983452A		34	1	31	0	2	FALSE	87	1	1	5	2	1	3	2	1	2	3	3	2	2	4	5	1	1	2	2	99	99	3	3	2	2	99	99	5.18		4.72		10	2	62	40	16	25	69
4	GOPAL MAJI	001145D		24	1	24	0	3	FALSE	78	1	1	4	2	5	2	2	2	4	2	3	3	3	5	3	2	2	2	2	2	2	3	3	2	1	3	2	5.75		4.2		10	1	80	2	8	25	80
5	UTTAM KHAN	294557C		41	1	23	0	1	FALSE	127	1	1	4	3	2	3	4	1	4	1	3	4	2	4	2	1	1	2	2	1	1	2	2	2	3	1	1	9.73		8.26		10	1	78	16	8	22	66
6	SIBARAM KHAN	207833D		41	1	99	0	3	FALSE	68	1	1	3	99	1	1	3	2	3	2	2	4	4	3	2	1	1	2	2	3	3	2	2	3	3	3	4	8.81		7.3		10	1	62	18	12	26	82
7	PUSHPA.V	412098B		46	2	99	0	2	FALSE	51	1	1	5	2	5	1	1	2	2	3	2	3	3	4	5	2	1	1	1	99	99	3	2	3	3	99	99	11.25		5.06		10	6	84	40	4	12	32
8	MOHIT BANERJEE	423580D		52	1	99	3	2	TRUE	59	1	1	3	2	1	3	2	4	3	1	4	3	5	4	3	2	1	2	2	2	2	2	2	2	3	2	3	8.3		6.13		10	2	72	28	9	24	75
9	DILIP BAURI	560931D		40	1	21	1	2	FALSE	55	1	1	4	99	3	2	2	1	3	3	2	2	1	5	4	2	2	2	2	2	2	2	2	2	2	3	3	9.23		5.9		10	4	72	18	9	22	59
10	MONARANJAN JANA	790977D		54	1	99	0	99	FALSE	27	1	1	4	99	1	3	2	3	3	3	3	3	3	4	4	2	2	3	3	2	1	3	2	3	3	3	2	9.71		9.3		8	0	28	10	20	28	88
11	ANU PRAVA DEY	721626D		50	1	30	2	2	FALSE	51	1	1	4	99	1	3	1	2	4	2	3	2	3	5	3	1	1	1	1	99	99	1	2	2	1	99	99	7.84		7.59		10	1	84	24	13	28	93
12	ARVIND KUMAR SINGH	381376D		36	1	99	0	99	FALSE	41	1	1	5	99	1	1	1	1	1	5	2	2	2	2	5	1	1	1	1	99	99	2	2	2	2	99	99	7.58		4.69		10	6	40	20	14	20	40
13	MUZAMMIL HUSSAIN.	891751C		36	1	99	0	2	FALSE	164	1	1	3	1	1	1	1	3	4	1	2	3	4	4	2	1	1	1	1	1	1	2	2	2	2	2	2	9.14		8		10	2	90	20	0	14	48
14	VELAYUTHAM P	532297C		36	1	24	1	99	FALSE	56	1	1	4	99	5	2	2	2	4	1	3	3	4	5	1	1	1	2	1	2	1	2	2	2	2	2	2	7.87		6.94		10	2	66	18	10	25	75
15	TAPAN SARKAR	033966D		46	1	25	0	99	FALSE	70	1	1	4	1	1	1	1	2	3	2	1	2	3	3	3	2	2	2	2	1	1	2	2	2	2	2	1	11.4		9.63		10	2	80	12	5	26	87
16	ANIL KUMAR BHATTACHA	590787C		48	1	23	1	1	FALSE	58	1	1	4	1	3	3	2	1	4	1	4	3	2	5	2	2	2	2	2	2	2	2	3	3	2	2	2	10.2		8.8		10	1	76	4	7	28	100
17	RAJKUMAR ROY	612910D		36	1	99	0	1	FALSE	48	1	1	3	2	99	3	2	3	1	4	3	3	3	1	4	1	1	2	2	1	1	2	2	3	4	3	3	9.45		9.22		10	2	52	6	13	27	87
18	ARUMUGAM.P	960192C		46	1	24	0	1	FALSE	84	1	1	4	2	5	3	3	3	2	2	4	4	4	3	4	2	2	2	2	3	2	3	2	2	2	3	2	12.56		10.32		10	4	98	58	2	11	33
19	DILIP KUMAR MANDAL	368323C		42	1	99	0	2	FALSE	127	1	1	4	2	1	2	2	3	3	2	2	2	4	5	2	2	2	2	2	2	2	2	1	2	3	2	3	8.72		5.6		10	1	80	10	6	24	78
20	GOUTAM HAZRA	097901C		26	1	18	0	99	FALSE	53	1	1	4	2	1	2	1	1	3	2	2	2	1	4	4	1	1	2	2	2	2	2	2	2	2	2	2	8.16		7.51		10	2	64	20	15	21	42
21	JAYAKANTHAN	912577B	CE	45	1	25	0	2	FALSE	60	99	1	4	2	5	2	2	1	4	1	2	3	3	4	1	2	2	2	2	2	2	3	3	3	3	3	3	9.2		8.42		10	1	74	14	8	26	85
22	BASUDEV SAHU	986078D		42	1	22	2	2	FALSE	36	1	1	4	2	4	1	1	3	3	1	1	1	4	5	1	2	2	2	2	1	1	2	2	2	2	2	2	11.91		8.6		10	4	48	32	13	21	50
23	RAM SUNDAR SINGH	088583D		61	1	99	2	1	FALSE	82	1	1	3	99	1	1	1	1	1	1	3	3	4	2	3	2	2	2	2	1	1	2	3	3	2	2	2	10.4		6.89		10	8	96	29	6	10	17
24	SUK DEB MONDAL	233749D		45	1	26	0	2	FALSE	74	1	1	4	2	99	2	2	1	3	1	3	3	2	3	1	1	1	2	1	2	2	2	2	3	2	2	2	8.13		7.71		10	1	68	10	4	26	88
25	NITHIYANANDAM K	084846D		45	1	25	0	2	FALSE	78	1	1	3	2	5	3	3	2	3	1	4	4	4	4	1	1	1	2	2	1	1	1	1	2	3	1	1	11.78	99	7.97		10	2	76	12	8	24	76
26	SUMITRA SARKAR	201445D		24	2	99	0	1	FALSE	70	1	1	4	99	99	2	2	3	4	3	2	2	4	5	4	3	2	2	1	99	99	3	2	2	2	99	99	5.91		3.41		10	1	74	18	8	26	85
27	NAYEM GAZI	912486C		35	1	27	0	99	FALSE	87	1	1	5	1	5	1	1	1	3	4	1	1	1	4	5	2	2	2	2	99	99	2	2	2	2	99	99	8.74		6.76		10	4	88	36	6	19	56
28	CHANDAN CHOWDHURY	289402D		37	1	99	0	2	FALSE	61	1	1	4	2	1	2	2	2	4	3	2	2	2	5	4	2	2	2	3	2	2	2	3	2	3	2	3	6.81		7.3		10	2	76	16	9	25	80
29	BHAGABATI MANDAL	932738C		49	2	23	0	2	FALSE	70	1	1	5	1	1	1	1	1	1	5	2	2	2	2	5	2	2	1	1	99	99	2	2	2	2	99	99	9.34		7		10	3	96	20	7	25	81
30	SWAPAN BERA	626988D		53	1	99	0	2	FALSE	47	1	1	4	99	4	2	1	1	4	2	2	1	1	4	2	2	2	4	2	1	1	2	2	4	3	2	1	7.44		5.72		10	2	64	24	10	20	52
31	ANNAMALAI R.	825817B		44	1	25	0	1	FALSE	103	1	1	4	1	5	2	3	4	5	4	3	3	4	5	4	2	2	3	2	2	2	2	2	3	3	2	3	4.08		2.58		10	2	98	54	6	16	43
32	BISWANATH MANDAL	828536D		37	1	24	0	1	FALSE	37	1	1	5	2	99	2	1	1	1	4	2	1	1	1	4	3	2	2	2	99	99	3	2	2	2	99	99	7.37		6.55		10	1	56	8	4	28	96
33	SHANTHI T.	881093D		39	2	23	0	2	FALSE	34	1	1	4	1	5	1	1	3	3	1	1	1	3	4	1	1	1	1	1	1	1	2	2	2	2	2	2	8.74		8.01		10	2	84	16	8	25	80
34	ANJANA GHOSH	200534D		36	2	99	0	2	FALSE	51	1	1	5	99	1	2	2	1	3	4	2	2	1	3	4	2	2	1	2	99	99	2	2	2	2	99	99	8.41		6.89		10	1	38	10	18	24	54
35	SUPHAL KANTI SARMA	201824D		30	1	21	0	2	FALSE	39	1	1	3	99	1	2	2	3	3	1	2	2	4	4	2	99	99	2	2	2	2	99	99	2	2	3	2	9.12		8.87		10	2	86	26	7	22	68
36	MATUR KUNDU	184099D		50	1	24	1	1	FALSE	60	1	1	5	99	1	1	1	2	3	5	1	1	3	4	5	2	2	2	1	99	99	2	2	2	2	99	99	4.39		3.5		10	1	48	4	6	27	91
37	ANIP PAL	511230D		38	1	27	0	2	FALSE	40	1	1	5	99	1	1	1	1	2	3	1	1	1	3	4	2	1	2	1	99	99	2	1	2	1	99	99	6.73		5.9		10	2	60	24	10	22	63
38	TAPAN SUTRA DHAR	180824D		39	1	99	0	2	FALSE	61	1	1	4	99	1	1	1	1	3	1	2	1	1	4	2	2	3	2	2	2	2	2	2	2	2	2	2	10.7		9.68		10	6	58	35	16	20	30
39	MANIK CHATTERJEE	601488D		55	1	19	0		FALSE	50	1	1	5	2	4	2	3	3	3	4	3	3	3	4	5	2	2	1	1	1	1	2	2	2	2	1	1	7.18		6.79		10	1	82	8	9	25	80
40	KAUSIK JANA	653494D		35	1	22	0	3	FALSE	48	1	1	5	2	1	2	2	3	1	4	2	2	3	2	5	2	2	2	2	99	99	2	2	2	3	99	99	6.74		4.89		10	2	96	49	6	18	52
41	PARIMALA.U.	761349C		35	2	28	0	2	FALSE	77	1	1	5	99	4	1	1	1	2	4	3	2	2	4	5	2	2	2	2	99	99	2	2	2	2	99	99	6.5		5.05		10	2	86	34	8	22	66
42	DEBANAND MAITI	706434D		32	1	20	0	1	FALSE	43	1	1	5	2	4	3	3	2	3	3	4	4	3	4	5	2	2	2	2	99	99	2	2	2	2	99	99	7.15		6.79		10	1	82	2	9	29	100
43	SALAI REVATHI K.	217951D		28	2	29	0	2	FALSE	74	1	1	4	2	3	2	2	1	4	5	2	2	1	4	5	2	2	1	1	99	99	2	2	2	2	99	99	7.72		8.99		10	3	64	30	7	21	63
44	ARUN K.	699473D		35	1	24	0	2	FALSE	50	1	1	4	2	5	1	1	1	4	1	1	1	1	4	1	2	2	2	2	2	2	2	2	2	2	3	3	11.5		11.32		10	3	50	4	16	26	83
45	JABAPATRA	853620C		37	2	23	0	3	FALSE	97	1	1	5	99	3	1	1	1	1	2	1	1	1	1	2	1	1	2	2	99	99	1	1	2	2	99	99	9.39		5.86		10	6	92	60	4	11	28
46	SOUMALYA BANERJEE	763633C		22	1	26	0	2	FALSE	103	1	1	4	2	1	1	1	1	3	3	1	1	1	4	3	2	2	3	2	2	2	2	2	3	2	2	2	8.21		8.57		10	1	68	4	9	28	95
47	SUDHIR NATH	035948D		31	1	22	0	1	FALSE	60	1	1	4	1	1	1	1	1	3	2	1	1	1	4	2	2	2	3	3	2	2	2	2	3	3	2	2	9.66		9.1		10	2	64	2	11	25	77
48	SANJAY GHARAI	960820D		35	1	20	3	1	TRUE	35	1	1	4	99	4	1	1	3	4	1	1	1	4	4	1	2	2	2	2	2	2	2	2	3	2	2	2	6.73		6.47		10	6	80	52	5	21	66
49	ASHOK KUMAR	388728C		39	1	26	0	1	FALSE	84	1	1	5	2	5	1	1	1	1	4	2	2	1	1	5	2	2	2	2	99	99	2	3	2	2	99	99	8.4		8.4		10	4	78	44	6	29	56
50	ARATI ACHARIYA	691438C		37	2	99	3	99	FALSE	88	1	1	5	99	1	2	2	1	1	4	2	2	1	1	5	1	1	1	1	99	99	1	1	2	2	99	99	8.05		4.43		10	5	76	64	12	19	41
51	RUPALI KUNDU	019036D		35	2	99	0	3	FALSE	72	1	1	4	99	1	1	1	2	3	1	1	1	2	4	1	2	2	3	2	2	3	2	2	3	2	2	3	12.36		11.03		10	8	72	66	10	11	5
52	RAJA	214109D		36	1	24	0	1	FALSE	75	1	1	4	2	1	1	1	2	3	3	1	1	3	4	4	2	2	3	2	2	2	2	2	3	2	2	2	8.6		7.51		10	1	86	4	5	26	87
53	MURTHY	567530D		36	1	21	0	1	FALSE	24	1	1	4	99	1	1	1	1	2	1	1	1	2	4	1	2	2	2	2	2	2	2	2	2	2	2	2	10.2		9.2		10	5	78	30	12	19	41
54	APARNA MONDAL	005365D		21	2	24	0	3	FALSE	87	1	1	4	99	1	1	2	1	2	1	1	2	2	3	1	1	1	1	1	1	1	99	99	99	99	99	99	10.89		9.56		10	2	96	18	5	24	79
55	DEBASISH MITRA	917308C		30	1	23	0	2	FALSE	92	1	1	4	2	1	1	1	1	3	1	1	1	1	4	1	1	1	1	1	2	1	1	1	1	1	2	1	10.37		7.21		10	2	66	8	9	27	90
56	VIJAYALAKSHMI	713111B		42	2	22	1	3	FALSE	84	1	1	5	2	1	1	1	1	2	4	1	1	1	3	5	2	2	2	2	99	99	2	2	2	2	99	99	6.12		4.02		10	1	86	14	7	26	86
57	EKAMBARAM	289774B		72	1	24	1	2	FALSE	72	1	1	5	2	5	2	2	2	2	3	3	3	3	3	4	2	2	2	3	99	99	2	2	2	3	99	99	8.56		7.68		10	0	66	6	13	29	100
58	RANGANATHAN	237391C		58	1	20	3	2	FALSE	73	1	1	5	99	1	1	1	1	2	2	1	1	1	2	4	2	2	2	3	99	99	2	2	2	3	99	99	7.16		5.23		10	3	42	18	16	24	61
59	SUFAL KUMAR SARKAR	435177D		28	1	27	0	2	FALSE	65	1	1	5	2	1	1	1	1	1	4	1	1	1	1	5	2	2	2	2	99	99	2	2	2	2	99	99	6.47		6.39		10	0	84	4	15	26	78

NO	NAME	H.NUM	SUBDIAGNOSIS	AGE	SEX	BMI	COM	OCC	SMOKE	FU	DX	SX	OPS	PY	DOC	PGR1	PGR2	PGR3	PGR4	PGR5	PGO1	PGO2	PGO3	PGO	PGO5	CPL	CPR	ASL	ASR	CDL	CDR	CPL	CPR	ASL	ASR	CDL	CDR	DHPRP	DHPOP	DHFU	FUS	VASR	VASO	ODIR	ODIO	JOAR	JOAO	HRR
1	CHHANDA KAR	183947D	Degenerative-2	66	2	27	0	99	FALSE	62	2	2	4	99	1	3	3	3	5	2	4	4	4	0	4	2	3	2	3	1	2	2	3	99	99	2	3	5.3	11.02	10.2	2	10	4	76	22	13	19	37
2	DESINGH R	960962D	Isthmic-2	66	1	26	0	1	FALSE	34	2	2	5	2	1	1	2	3	2	5	1	1	3	3	5	2	2	3	2	99	99	3	2	99	99	99	99	6.25	5.74	4.55	4	10	5	52	44	9	16	35
3	ALAKA MAITI	833218D	Dysplastic-2	56	2	28	2	2	FALSE	38	2	2	5	1	4	1	1	1	1	4	1	3	2	2	5	3	3	3	3	99	99	4	3	99	99	99	99	6.44	11.63	11.44	1	10	2	82	14	5	25	83
4	MARIAMMA ABRAHAM	317821D	Degenerative-1	53	2	31	3	2	FALSE	54	2	2	4	1	2	1	2	3	3	1	2	4	4	0	2	2	3	2	3	2	3	2	3	99	99	3	3	12.14	14.39	12.54	2	10	2	76	16	8	22	66
5	KHOKAN KHAN	634157C	Dysplastic-4	42	1	99	0	1	TRUE	94	2	2	5	2	5	1	1	1	2	5	1	1	1	3	0	3	2	2	2	99	99	3	4	99	99	99	99	6.91	10.69	7.7	1	10	1	72	4	2	27	92
6	NAWSHAD BEGAM J.	640774D	Tuberculous Spond	44	2	99	0	3	FALSE	33	3	2	5	2	1	1	1	1	1	5	3	3	3	3	0	3	3	4	3	99	99	4	3	99	99	99	99	5.95	7.71	4.66	3	10	4	86	34	16	20	30
7	MANI M	646468D	Degenerative-1	55	1	20	2	2	FALSE	52	2	2	4	2	5	1	3	3	4	1	2	3	4	0	1	2	2	4	4	3	3	2	2	99	99	3	4	5.24	13.43	8.96	3	10	4	86	38	8	15	33
8	DHANANJOY GHOSH	787808B	Dysplastic-3	47	1	99	3	1	TRUE	92	2	2	5	99	4	1	1	1	1	5	1	2	3	3	0	2	2	4	3	99	99	3	4	99	99	99	99	9.01	8.52	0	1	10	2	76	32	11	22	61
9	SABILA KHATUN	349378C	Degenerative-1	48	2	99	0	2	FALSE	101	2	2	4	99	1	2	2	3	5	2	3	3	3	5	3	2	3	3	3	2	2	2	4	99	99	2	2	5.16	6.25	3.01	3	10	2	62	28	10	25	78
10	PRATIMA MAHTO	762321C	Degenerative-1	49	1	31	0	2	FALSE	60	2	2	3	99	4	2	3	3	2	1	3	4	4	3	2	2	2	3	3	2	2	2	2	99	99	3	2	7.01	10.4	10.74	4	10	3	80	14	11	27	88
11	SANTHAKUMARI N.	254292C	Degenerative-1	48	2	29	2	2	FALSE	58	2	2	4	1	4	1	1	1	3	1	2	2	2	5	2	2	3	3	4	2	3	3	4	99	99	4	4	8.52	11.5	11	3	10	5	64	56	15	17	14
12	SHOVA RANI HALDER	424670D	Degenerative-2	34	2	26	0	2	FALSE	49	2	2	4	2	1	1	1	1	4	3	1	2	2	5	4	2	2	4	4	1	2	2	2	99	99	2	2	7.08	10.13	5.13	3	10	1	70	10	8	27	90
13	UMA GHOSH	564926D	Degenerative-1	41	2	99	3	2	FALSE	999	2	2	4	99	4	2	2	2	4	1	2	2	4	5	1	2	1	2	2	1	1	2	2	99	99	2	2	6.46	8.35	6.84	4	10	0	46	2	14	27	86
14	LAXMINARAYAN LENKA	176074D	Infective Spondyloc	44	1	25	3	3	TRUE	77	3	2	5	2	1	1	1	1	1	5	1	2	3	3	0	2	3	2	3	99	99	3	4	99	99	99	99	4.17	9.66	0	1	10	1	92	4	6	28	95
15	SAMBURNAM	069819D	Dysplastic-1	62	2	23	2	3	FALSE	86	2	2	4	2	5	1	1	1	1	4	1	1	1	2	0	2	3	1	2	99	99	3	3	99	99	99	99	6.11	7.15	0	1	10	1	90	14	6	27	91
16	VENDAMMAL	969955C	Degenerative-1	43	2	23	0	3	FALSE	84	2	2	4	2	5	1	1	2	4	2	2	2	2	0	3	2	2	4	4	3	2	3	3	99	99	3	2	7.6	10.92	0	1	10	5	68	38	9	19	50
17	MAMATA SHAW	725760D	Dysplastic-2	46	2	32	3	3	FALSE	48	2	2	4	2	1	2	1	1	5	3	3	2	2	5	4	1	1	2	2	1	1	2	2	99	99	1	1	3.82	13.52	11.02	2	10	2	64	18	15	25	71
18	JAYANTA BANERJEE	293560D	Infective Spondyloc	43	2	99	0	2	TRUE	28	3	2	3	1	2	3	3	4	1	1	3	3	0	3	2	1	1	2	2	2	2	2	2	99	99	3	3	8.92	16.24	0	1	10	1	60	4	11	27	88
19	VASANTHA	335218D	Degenerative-1	47	2	33	3	3	FALSE	45	2	2	4	99	1	1	1	1	3	2	2	2	2	0	3	2	2	4	2	2	2	4	3	99	99	2	2	8.62	13.17	8.4	2	10	2	72	38	10	24	73
20	JOY DEB GHOSH	381154C	Discitis	34	1	18	0	1	FALSE	115	1	2	4	2	1	2	2	2	5	1	2	2	2	5	3	3	3	3	3	2	2	4	4	99	99	3	4	4.73	6.86	5.44	3	10	2	44	12	15	27	85
21	SHOVA SAHOO	042005D	Isthmic-2	44	2	99	0	2	FALSE	52	2	2	4	2	1	1	1	1	5	1	1	1	1	5	1	3	3	3	3	2	2	3	3	99	99	3	3	4.76	11.29	7.1	4	10	8	16	32	16	14	53
22	UMA DEVI	504751D	Degenerative-1	67	2	21	2	1	FALSE	47	2	2	4	99	99	2	2	1	5	1	3	3	2	0	1	1	1	2	3	2	3	2	2	99	99	3	4	6.51	14.69	12.35	2	10	2	64	40	8	18	47
23	RAJESWARI	313885B	Isthmic-2	47	2	99	3	3	FALSE	35	2	2	5	2	5	2	1	1	0	5	2	1	2	0	5	3	3	3	2	99	99	2	3	99	99	99	99	8.26	10.2	10.2	2	10	2	74	10	6	28	95
24	GOBINDA DEVI	259335D	Degenerative-1	60	2	33	3	99	FALSE	62	2	2	4	99	5	2	2	2	3	2	3	2	2	0	2	3	3	4	4	4	3	3	4	99	99	4	3	11	12.7	11.4	2	10	4	94	62	6	17	47
25	GHOSH B.C	292937C	Degenerative-1	70	1	99	2	2	FALSE	68	2	2	4	99	1	2	3	3	5	3	2	3	3	0	3	1	1	3	4	2	3	99	99	99	99	99	99	5.02	13.92	10.45	2	10	2	88	24	12	24	70
26	ARUNDHATI SEN	714749D	Degenerative-1	45	2	24	0	1	FALSE	51	2	2	4	2	1	1	1	2	4	1	2	2	3	0	1	2	3	2	3	1	1	99	99	99	99	99	99	6.39	12.28	8.97	2	99	99	58	28	16	18	28
27	SUNIL PAL	556506D	Infective Spondyloc	48	1	99	0	1	FALSE	37	3	2	4	99	1	2	2	3	5	1	3	3	3	0	1	3	3	4	3	2	3	3	3	99	99	3	3	7.12	8.6	0	1	10	0	86	14	16	26	76
28	CHANDRASEKHAR	013973D	Dysplastic-1	30	1	99	0	1	FALSE	66	3	2	5	99	5	1	1	1	2	5	1	1	1	3	0	3	3	3	4	99	99	3	3	99	99	99	99	7.97	9.21	10.69	2	10	2	76	24	16	22	46
29	SRUTI DAS	956417C	Degenerative-1	54	2	23	3	2	FALSE	88	1	2	4	1	1	2	3	2	5	1	3	4	4	5	3	2	3	4	4	1	1	2	3	99	99	1	1	4.87	10	8.36	3	10	4	72	28	6	20	60
30	MAHAMAYA MUKHERJEE	376224D	Isthmic-1	45	2	27	3	2	FALSE	59	2	2	4	1	4	2	1	1	5	3	3	3	2	0	3	2	2	3	2	3	3	2	2	99	99	3	3	3	9.6	4.52	2	10	2	98	18	3	22	73
31	MEHERTAJ BEGUM	422448B	Isthmic-1	39	2	29	0	3	FALSE	50	2	2	5	99	4	2	1	1	1	4	2	1	1	1	0	1	1	2	1	99	99	3	3	99	99	99	99	7.31	9.04	8.58	2	10	3	60	40	12	19	41
32	SHIBNATH MONDAL	598109D	Isthmic-1	46	1	99	0	2	FALSE	48	2	2	4	99	1	2	2	1	1	4	2	2	1	1	5	2	3	3	3	99	99	3	3	99	99	99	99	11.19	16.3	12.12	3	10	2	74	38	7	21	66
33	SHYMALI JALUA	116250C	Isthmic-2	47	2	99	0	3	FALSE	84	2	2	4	99	1	1	1	2	4	3	1	1	2	0	3	1	1	1	3	1	3	3	2	99	99	2	3	7.5	12.59	8.29	3	10	4	60	48	18	20	18
34	RIYAZ AHMED	680134A	Degenerative-1	45	1	24	3	2	TRUE	94	2	2	4	2	5	2	3	3	4	1	3	3	3	5	1	3	2	4	2	3	3	3	4	99	99	4	3	9.22	13.05	8.47	4	10	1	70	8	10	27	89
35	KANAI LAL PRADHAN	825195C	Isthmic-1	47	1	20	3	1	TRUE	99	2	2	4	1	5	4	2	3	5	2	4	3	3	0	2	2	2	3	2	3	3	2	3	99	99	3	4	4.42	9.12	0	1	10	1	76	2	7	28	95
36	RAMASWAMY	820275A	Dysplastic-1	46	1	27	3	2	FALSE	73	2	2	4	99	1	3	3	2	3	3	3	3	3	4	4	2	2	3	4	3	4	2	2	99	99	3	4	10.2	11.85	10.63	4	10	2	64	18	13	22	56
37	RAJATHI	789929B	Degenerative-1	37	2	28	0	3	FALSE	37	2	2	4	2	5	2	1	1	4	1	3	2	1	5	1	2	3	2	4	2	2	2	3	99	99	3	3	5.7	9.61	9.24	3	10	5	74	28	3	14	42