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Pathomechanisms, Pathophysiology and Biomechanics of Degenerative Spine Disease: A Review of Literature

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ABSTRACT

The intervertebral disc in human being is a complex structure and is made up of fibrous and cartilaginous tissues. It is characterized as tension-resisting structure while it allows limited range of motion in axial, bending or rotational posture. Degenerative process of this structure present with clinical morbidity to the patients and possess great challenges to the clinicians while offering care for disc's pathology. Degeneration begins with imbalance of homeostasis maintained by content of nucleus pulposus and annulus fibrosus. Numerous factors; genetic, mechanical and nutritional, can initiate and or accelerate this degeneration process which ultimately alter the biomechanics of the spine. The aim of this review is to give an overview on the degeneration process, causes and factors influencing disc degeneration, the mechanisms of degeneration and the changes resulted from intervertebral disc degeneration.

KEYWORDS: intervertebral disc, disc degeneration, biomechanisms, spine, low back pain

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INTRODUCTION

The degenerative disc disease (DDD) of the lumbar vertebra and low back pain (LBP) are chronic conditions with many causes. It is also an important cause of morbidity and death in everyday clinical practice (1). Chronic LBP is one of the leading causes of disability and imposes a huge social, medical, and economic stress worldwide, especially in the young and active population. (2) Aetiology is known but not always clear; the low back pain often results from the pathology of an intervertebral disc, sacro-iliac and facet joints, and soft tissues (3)

Hoy et al. (2008) conducted a comprehensive study on the worldwide occurrence of Low Back Pain (LBP) and found a prevalence of 11.9 ± 2.0%, a one-year prevalence of about 38.0 ± 19.4%, and an average long time, over life existence prevalence of 39.9 ± 24.3%. (4) The authors showed a clear positive relationship between the average occurrence of lower back pain and a country's human development index. However, they did not find a significant variation in incidence between rural and urban areas. Ravindra et al. conducted a study in 2018, revealing that patients with degenerative lumbar disease and chronic LBP are three times more common in low- and middle-income nations compared to high-income countries. (5) Freburger et al. reported a notable rise in the occurrence of chronic low back pain over 14 years, with symptom intensity and overall health status remaining constant. (6) The increase in the occurrence of lower back pain may be due to the current increase in important risk factors such as obesity, lack of sleep, and chronic stress. (7) Additional notable risk factors linked to lower back pain are smoking and work dangers, including heavy lifting and improper posture. (8)

Treatment modalities such as physiotherapy, painkiller medication, and corticosteroid usage are often employed for reducing intervertebral disc (IVD) pain. (9, 10)
It should be noted that neither surgical nor non-surgical interventions ensure complete resolution of the underlying pathology. To prevent continuous degeneration and promote IVD regeneration, biological treatments such as gene therapy, growth factor and cell injections, and tissue-engineered approaches such as nucleus pulposus (NP) augmentation, annulus fibrosus (AF) repair, and total disc replacement have been extensively studied. (11, 12)
Although most innovative medicines are limited to laboratory experimental
models, there has been an increase in clinical studies during the past decade. (13) Understanding the underlying pathomechanism is critical for developing novel, safer, and more effective therapies. This review aims to present complete data on the prevalence of LBP and DDD, emphasizing the need for novel biological treatment options.
A literature search was done for this review. Data about intervertebral disc anatomy, degeneration, and its effects was gathered from multiple sources. These included online databases; PubMed, Medline, and Science Direct. The search words included IVD, DDD, fibrous annulus, nucleus pulposus, and lumbar spine. Articles were chosen based on their scientific merit and alignment with the study's purpose.

Anatomy of the Intervertebral

The intervertebral disc is a complex organ made up of fibrous and cartilaginous connective tissues that act as a separation between two adjacent vertebrae. It allows for a limited range of torso mobility while also providing stability during axial compression, rotation, and bending. (14) An IVD is made up of three parts: an inner gelatinous NP, an outer AF, and cartilage end plates positioned above and below. The outer annulus fibrosus, which is rich in type I collagen, is a circular layer that resists tensile strength because the collagen fibers run obliquely between the annulus' lamellae in alternate directions. The nucleus pulposus is made up of a proteoglycan and water gel that are merely kept together by irregular networks of fine type II collagen and elastin fibers. Aggrecan is the primary proteoglycan in the nucleus pulposus, and it offers the osmotic characteristics required to resist compression. The intervertebral disc is among the largest avascular tissues in the body. (15) Disc tissues obtain their nutrition from arteries in the subchondral bone next to the hyaline cartilage of the end plate. Small molecules, such as glucose and oxygen, are conveyed through the end plate in a passive diffusion process. The cells in the disc regulate the biological metabolism of the discs by managing several materials, such as cytokines, enzymes, and growth factors. (16)
In fetal and juvenile discs, the distinction between the annulus fibrosus and nucleus pulposus regions is obvious. (17) In adult discs, however, the outer nucleus pulposus passes seamlessly into the inner annulus fibrosus, rendering the boundary between the two regions indiscernible due to their comparable matrix compositions. In contrast to the round chondrocyte-like cells of the mature outer nucleus pulposus and inner annulus fibrosus, the cells found in the outer annulus fibrosus layers are elliptic and fibroblast-like. (18)
The vertebra endplates, which line the superior and inferior surfaces of both the nucleus pulposus and annulus fibrosus, are made up of two separate layers: the cartilage endplate, which is composed of Type II collagen and aggrecan, and the bony endplate, which is composed of cortical bone. The cartilage endplate parts of healthy vertebra endplates are consistent in thickness and do not infiltrate adjacent vertebrae. (19) In contrast to the 27:1 proteoglycan-to-collagen ratio of the nucleus pulposus, the ratio is 2:1 in the hyaline cartilage of the cartilage endplates. (20) Vertebra endplates perform two functions: one as an attachment between the disc and the vertebra and the other as a pathway for material delivery to the disc. Because vascularity is restricted to the outside edges of the cartilage endplate, nutrients and oxygen eventually reach the annulus fibrosus and nucleus pulposus areas by passive diffusion. (21) A healthy intervertebral disc is mostly aneural, with the exception of the outer annulus fibrosus layers, which are innervated by sensory and sympathetic perivascular nerve fibers. (22) Neoinnervation reaching into the inner intervertebral disc differentiates healthy from degenerative discs.

Pathophysiology

Degenerative disc disease is caused by a breakdown in the homeostasis, which is maintained by the intervertebral disc structures, with genetic and environmental variables believed to accelerate disease progression. (22,23) Multiple studies have found various risk factors associated with degenerative disc disease, and these include genetics, obesity, smoking, and ageing (24); however, the influence of each risk factor on degenerative disc disease progression is yet unknown. In 2008, research found 34% to 61% heritability rates for degenerative disc disease, indicating a complex inheritance pattern involving several genes. (25) Additionally, there are discrepancies in the growth differentiation factor (26). Several genes, including vitamin D receptor and matrix degradative protease, have been associated with intervertebral disc disease, although their impact on the disease remains unknown. Mutations in genes encoding Type II collagen, a key component of the nucleus pulposus and inner annulus fibrosus extracellular matrix, and Type XI collagen have been linked to vertebral endplate deformations but not degenerative disc disease. (27)

Several studies have connected SNPs on the COL1A1 genes to degenerative disc degeneration. (28)

Solovieva et al. found that obesity and changes in collagen type IX (COL9A3) increase the severity of degenerative disc degeneration, as seen by decreased disc heights and weaker MRI signals of the nucleus pulposus. (29) Polymorphisms in aggrecan genes have been linked to degenerative disc disease by affecting the length of core proteins and the quantity of chondroitin sulfate chains bound to aggrecan. (30) A decrease in chondroitin sulfate chains affects the nucleus pulposus' ability to hold water, resulting in decreased disc height and enhanced neoinnervation. (31)

Obesity, smoking, and ageing are other major risk factors for degenerative disc disease. Samartzis et al. found that overweight and obese persons had a higher severity of degenerative disc disease compared to underweight and normal BMI individuals in a population-based study of juveniles aged 13-20. (32) Overweight and obese persons have excessive compressive stresses on their discs, which can lead to early wear and tear and worsen preexisting degenerative disc disease. (33)

Disc degeneration process

Mechanical factors, including duration, severity, type, and position of load, impact the state of the intervertebral disc and its biological response. (34, 35)As an organism grows, the border between the annulus and nucleus becomes more pronounced. Degenerative processes involve structural damage and changes in cell number and composition, with the nucleus being primarily affected by aging. (35) IVD gets less elastic and more fibrous as time goes on and extends into the nucleus from the outermost section of the disc, where it originates from the tiny concentric ruptures that form there. (34) Fibrous tissue degeneration occurs due to factors like mechanical, traumatic, genetic, and nutritional damage. (36) Fibres in the fibrous annulus become disoriented, and the network of elastin and collagen fibers deteriorates. Cells in the nucleus undergo apoptosis and necrosis with excessive proliferation. These degenerative cascades are frequent, with up to 50% of cells in an adult intervertebral disc potentially necrotic. (37)

The degeneration of the intervertebral disc is primarily due to the loss of proteoglycans. (38) This further leads to a decrease in osmotic pressure and water loss, affecting the disc's mechanical properties. (39) Degenerated discs have less water, causing them to bulge and lose height. The loss of proteoglycans also affects the movement of other molecules into and out of the disc matrix, accelerating the degeneration process. (39)

Matrix degeneration affects collagen quantity and composition, with orientation, location, and types being the most affected. (40) Old collagen fibers denature, while new ones are synthesized during early degeneration. Enzyme activity, particularly matrix metalloproteinases and cathepsins, plays a crucial role in collagen, fibronectin, and proteoglycan denaturation and breakdown. (40,41)

Degenerative changes in the intervertebral disc, linked to damage to nearby structures like ligaments, joints, and vertebral muscles, increase injury susceptibility and lead to osteoarthritic degeneration, resulting in lower disc function and higher load-bearing joints. (40, 41)

Yellow ligaments' strength decreases, leading to hypertrophy and protrusion into the spinal canal, causing neural structures to narrow and compress. (42) Pain during degenerative processes is complex, involving structural and mechanical deformation, inflammatory mediator activity, and spinal nerve radices. Chronic pain is mainly caused by compression and ingrowth of tiny neural endings into the degenerated disc, triggered by constant inflammatory mediator release. (40,42)

Herniation is the bulging of the disc due to partial or complete rupture of the outer fibrous annulus, affecting the anterior, posterolateral, or posterior directions. (43) This can compress neural structures in the vertebral canal. (43, 44) Occasionally, a disc herniation may lead to lumbar pain relief. Typically caused by mechanical injury, initial degeneration is necessary for the pulpous nucleus to herniate through the annulus. (40, 44) A healthy disc ruptures with significant force, often due to vertebral plate failure. (45)

Factors influencing the intervertebral disc degeneration are discussed below;

Genetic/Hereditary factors

Genetic factors contribute to intervertebral disc degeneration. Genetic variations in matrix molecules can affect the extracellular matrix's integrity and the progression of degenerative diseases (46).

Mutations in genes that code for matrix components modify matrix shape, impacting disc function and biochemical processes (47). Intervertebral disc degeneration is likely a multifaceted illness, with environmental variables also contributing to its development (48).

Mechanical factors

Degeneration of the disc occurs as a result of the processes mentioned above, accelerated wear and tear of cellular and acellular components brought about by abnormal mechanical stresses and constant microscopic damage. When it comes to medical results, chronic pain is the most common. (49). Heavy physical labor, smoking (by atherosclerosis of small vessels that supply the terminal plates), obesity, awkward bent posture, and inactivity are the most significant risk factors (49).

Nutritional factors

The cells require an adequate quantity of nutrients to maintain the proper structure and function of the disc. So, nutritional imbalance of the intervertebral disc is also a major cause of

degeneration (50). The supply of the disc is mostly determined by diffusion because it is an avascular structure. The subchondral region of the disc terminal plate is the sole location to which capillaries that originate in the vertebral bodies extend. When nutrients are few, oxygen levels drop, lactate levels rise, and the pH changes, all of which have an impact on cellular processes and extracellular matrix production. The result is a degenerative process in the long run (51).

CONCLUSION

The causes and effective treatments for degenerative disc degeneration in the spine are a major medical mystery. Apart from non-operative and operative modalities, regenerative therapy shows great promise, but they are still under experiment. Through the use of growth factors that promote ECM synthesis by disc cells and medicines that inhibit cytokines, which often cause matrix degradation, regenerative therapy seeks to rebuild the deteriorated ECM. The distinction between aging changes and disc pathological degeneration remains unclear despite MRI examinations improving clinical understanding. Understanding the pathogenesis of disc degeneration will help in selecting treatment modalities and developing tissue engineering for biological restoration. Future treatments should aim for pain relief and biological reversal of the degenerative process, as structural failure of the disc does not always correspond to pain.

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