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REVIEW

Etiology for Degenerative Disc Disease

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Abstract Degenerative disc disease is a multifaceted progressive irreversible condition and an inevitable part of aging, which has been found to be a contributing factor for low back pain and might cause radiculopathy, myelopathy, spinal stenosis, degenerative spondylolisthesis, and herniations. Its etiology is complex and multifactorial. Although genetics influence more dominant, the occupational and mechanical influences still persist as a major risk factor. This review emphasizes up-to-date knowledge regarding etiology of disc degeneration with special consideration on occupational, lifestyle factors, and genetic polymorphisms.

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DEGENERATIVE intervertebral disc disease is an inevitable part of aging and found to be one of the contributing factors for low back pain.[1] Degenerative disc disease (DDD) affects the functional capability of intervertebral disc, making it unable to bear physiological loads, thus leading to damage to structural integrity, formation of disc herniation, osteophyte, and vertebral micro-fracture. Different methods have been used in the past to measure disc degeneration. The disc space height, signal intensity, and bulging are widely used to estimate degenerative changes of intervertebral disc based on computed tomography, magnetic resonance imaging (MRI), pathology, and autopsy results.[2-3] However, lack of uniform grading system of disc degeneration impedes progress in the understanding its etiology. DDD has been attributed to various factors such as physical loading, vehicular driving, spinal trauma, smoking, obesity, and genetic influences.[4-9] The pathogenesis of DDD and its association with environmental and genetic factors is poorly understood. In recent years molecular mechanism of DDD has been widely studied in the various populations. This review concentrates the latest advances on the evidenced factors associated with the occurrence of DDD.

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OCCUPATIONAL EFFECTS

Disc degeneration is highly linked to heavy physical loading specific to occupation. Occupational risk factors such as sustained abnormal postures, bending, vibration, twisting, sitting, heavy lifting, have been suspected to be associated with degeneration and herniation of intervertebral disc.[10-12] Elfering *et al*[13] reported that lack of exercise and night shift work were significant predictors for disc degeneration and its progression. In a cross-sectional MRI study, Luoma *et al*[1] found that low back pain was more

common among carpenters and machine workers than among office workers, but timing and signs of disc degeneration are unknown in this study. In another similar study Evans *et al*[14] revealed that frequency of degenerative change in lumbar intervertebral disc of sedentary women was high, whereas degenerative change was not found in ambulatory women. However men in this study showed no significance difference in prevalence of degenerative change in lumbar intervertebral disc. Lawrence[15] found that lumbar intervertebral disc degeneration was more general in miners and manual workers than in business and professional workers. Puustjarvi *et al*[16] noted strenuous exercise did not exert adverse influence on the intervertebral disc of young dogs.

Kelsey and Hardy[17] reported that individual who spends most of the time on driving vehicles tends to have more damage on intervertebral disc regardless of sex. This study also explained the prolonged sitting was associated with back pain or sciatica. Other studies also revealed that vehicle drivers are more prone to lumbar intervertebral disc degeneration than ones with other occupations.[12, 18, 19] Occupational drivers often have back problem and degenerative changes of intervertebral disc due to whole body vibration that caused by driving vehicle.[7, 20]

Although it is generally agreed occupational suspected risk factors play an important role in the pathogenesis of the degenerative process, a precise understanding of the biochemical and molecular events occurred in the disc that is exposed to prolonged sitting, heavy lifting, postural stresses and unpleasant environment remains elusive.

LIFE STYLE

Epidemiologic studies revealed smoking is a weak risk indicator but not a cause for disc generation.[21-23] Smoking has been identified to decrease blood flow to vertebral body,[24, 25] impair fibrinolysis,[26] raise intra-abdominal pressure because of coughing,[27] and reduce bone mineral content,[28-30] which might have direct or indirect effects on intervertebral disc degeneration. Kelsey *et al*[31] found no absolute difference between smokers and nonsmokers in cervical disc changes, and smoking plays little role in severity of disease. However, An *et al*[32] found smokers have higher risk for the cervical DDD than nonsmokers. Although nicotine-induced degenerative changes are irreversible, Nemoto *et al*[23] and Elmasry *et al*[33] regarded that smoking cessation is beneficial to regeneration of a degenerated disc to some extent.

Moreover, obesity or increased body mass index are closely related with disc degeneration.[6, 34, 35] One study in Japanese population demonstrated that degeneration among young adult men is associated with overweight and abdominal obesity.[34] Another study by Liuke *et al*[6] as well supported the above conclusion. However, a study of a small sample reported by Videman *et al*[36] did not find obesity was interrelated with disc degeneration based on signal variation on MRI. Prevention and control of obesity are given priority to lessen the severity of intervertebral disc degeneration.[6, 35, 37] However, more studies are needed to figure out the mechanism by which obesity and smoking increase the risk of DDD.

GENETIC FACTORS

Clearly, it is agreed that genetics, as a risk factor for DDD, has dominant influences on etiopathogenesis.[9, 38, 39] A case-control study performed by Matsui *et al*[40] suggested a strong familial predisposition to development of DDD. They observed significant disc degeneration in patients with a positive family history of disc herniation. Videman *et al*[41] examined 150 male twins who were scanned on MRI to record changes in the degenerative signs over a 5-year interval and found a prominent hereditary influences on the progression of DDD. In addition, they reported occupational factors had modest effects (from 2% to 15%) on development of DDD compared to genetic effects (from 47% to 66%). Another two studies on twins also revealed significant heritability influence on intervertebral disc degeneration.[38, 42] Moreover, environmental factors have been revealed to impact on disc signal variation among the twins in the two studies.

Predisposing genes such as vitamin D receptor (VDR), type I collagen (COL1), type IX collagen (COL9) A2 and COL9A3, aggrecan, have been proved to have strong relationship with DDD in several ethnic population.[43-46]

VDR

VDR, a member of nuclear steroid hormone receptor, is supposed to play an important role in normal bone mineralization and remodeling. Many disorders such as osteoporosis, osteoarthritis, and DDD are associated with gene polymorphisms of VDR.[47] Videman *et al*[44] described the association of DDD with VDR in monozygotic twins from Finland. A study of 205 Japanese young adults revealed that Tt genotype of VDR gene was more highly associated with DDD than TT genotype.[43] A large-scale study in Chinese by Cheung *et al*[47] further supported the link between t allele of VDR gene and DDD with an odds ratio of 2.61. Videman *et al*[48] concluded that individuals with tt genotype are more prone to suffer from annular rupture.