

ELECTRONIC LETTER

Association of a *COL1A1* polymorphism with lumbar disc disease in young military recruits

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Background: Lumbar disc disease (LDD), one of the most common conditions for which patients seek medical care, has been associated with sequence changes of the COL genes. *COL1A1*, however, has not been studied in young patients with LDD; *COL1A1* polymorphisms have been associated with bone mineral density (BMD) in several populations and with LDD in older adults.

Objective: To study *COL1A1* polymorphisms in young Greek army recruits with LDD.

Subjects: These young soldiers were diagnosed with early LDD at the time of their presentation to a military training site. All patients had radiological confirmation of their disease; a control group was also studied.

Methods: Sp1-binding site polymorphism of the *COL1A1* gene was investigated by standard methods.

Results: There was an increased frequency of the "ss" genotype (33.3%) in LDD patients; none of the controls had this genotype. In addition, a significantly smaller number of controls was heterozygotes for this allele.

Conclusions: A previously studied sequence change of the regulatory region of the *COL1A1* gene, the same as has previously been associated with low BMD in many populations and LDD in older adults, showed a strong association with LDD in young male soldiers who were recently diagnosed with this disease.

Lumbar disc disease (LDD) is among the most common ailments in Western societies.¹ In the military, LDD often results in significant impairments and contributes greatly to health care costs and disability.² Military training often results in exacerbation or presentation of LDD related symptoms. LDD appears to be a multifactorial disorder in which genetics play an important role, as it is evident from several recent studies.³

Collagen is the most abundant structural component of the extracellular matrix. Changes in collagen cross linking have been identified in degenerative disc disease, and LDD was recently associated with a polymorphism of the collagen type IX (*COL9A3*) gene.³ Type I collagen is the major protein in skin, ligaments, and bone; both *COL1A1* and *COL1A2* are present in the main components of the intervertebral disc, the annulus fibrosus (primarily) and the nucleus pulposus (secondarily).⁴

A G→T polymorphism within the *COL1A1* regulatory region that affects the recognition site for transcription factor Sp1 has been associated with lower bone mineral density (BMD), osteoporosis, and vertebral fractures mainly in postmenopausal populations.⁵ A recent paper in the *Journal of Medical Genetics* addressed the contribution of the Sp1 polymorphism in the determination of BMD in elderly white women.⁶ Although type I collagen abnormalities have been

Table 1 Genotyping data from patients with lumbar disc disease and controls

	Controls (n = 12)	Patients (n = 24)
Age (years)	25 (3.8)	29 (7.6)
Genotype		
G/G	4 (33.3%)	6 (25%)
G/T	8 (66.7%)	10 (41.7%)
T/T	0 (0%)	8 (33.3%)

implicated in the pathogenesis of LDD,⁴ the Sp1 sequence alteration has not been investigated in young patients with LDD.

METHODS

We collected blood from 36 Greek army recruits at the time of recruitment (during basic training), 24 with LDD (mean (SD) age, 29 (7.6) years), and 12 controls matched for body mass index (BMI) (mean age, 25 (3.8) years). All were healthy, with normal BMD and no history of trauma or fractures. The only health complaint of the patient group was low back pain. All patients had radiological confirmation of LDD by magnetic resonance imaging. The protocol was approved by the Department of Defence Health Service Review Committee, Athens, Greece.

Genomic DNA was extracted from blood samples by standard methods. To detect the G→T polymorphism, we used a polymerase chain reaction based method²; positive samples were sequenced for confirmation of the sequence change.

RESULTS AND DISCUSSION

There was a significant difference between patients with LDD and controls: 33.3% of the patients were T/T v none of the controls ($p < 0.001$) (table 1). In addition, a significantly smaller number of controls was heterozygotes for this allele: 66.7% in the LDD patients v 41.7% in the controls.

T is the "s" allele of the Sp1 binding site *COL1A1* polymorphism which has been associated with fractures, low BMD, and BMI.⁵ This is the second report of a positive association between the *COL1A1* "s" allele and LDD; the first, however, was a study of elderly patients with other bone diseases, in which it was shown that elderly men and women with the TT genotype had a higher risk of disc degeneration than those with the GG and GT genotypes, with an odds ratio of 3.6.⁷

It has been shown that the production of pro-collagen type I increases in LDD, possibly as a repair mechanism.⁴ Consistent with this hypothesis, a recent study suggested that collagen type I in a glycosaminoglycan matrix induced

Abbreviations: BMD, bone mineral density; LDD, lumbar disc disease

proteoglycans synthesis by canine intervertebral disc cells.⁸ In mice genetically engineered for reduced type I collagen, vertebral disc tissue was also mechanically inferior when compared with control animals.⁹ It is therefore plausible that an increased ratio of *COL1A1* expression compared with *COL1A2*—as suggested for the effect of this Sp1 binding site polymorphism⁵—may lead to structural alterations as well as to healing defects in the annulus fibrosus and other components of the discs in LDD.

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