ORIGINAL RESEARCH

Correlations of IL-6 and TGF-β Gene Polymorphisms and Expressions With Osteoporotic, Thoracolumbar, Vertebral Compression Fracture

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ABSTRACT

Context • Associations between genes and diseases manifest as the influence of gene expression on disease development as well as the impact of variations in the disease-related genes themselves. It's important to determine the genetic variations that can lead to compressed fractures of osteoporotic, thoracic lumbar vertebrae to develop personalized clinical methods to prevent or delay the disease's development.

Objective • The study intended to explore the correlations between the gene polymorphisms and gene expressions of the interleukin-6 (IL-6) gene and the transforming growth factor-beta (TGF-β) gene and osteoporotic, thoracolumbar, vertebral compression fracture.

Design • The research team performed an observational study using data from medical records.

Setting • The study took place at Xuzhou Medical University in Xuzhou, China.

Participants • Participants were 200 patients with an osteoporotic, thoracolumbar, vertebral compression fracture who had been admitted to the hospital at the university between 2019 and 2021 prior to the study and 200 healthy people The research team divided the participants into two groups. The patients became participants in the disease group, and the healthy individuals became participants in the control group.

Outcome Measures • The research team: (1) collected peripheral blood from the two groups, (2) extracted genomic deoxyribonucleic acids (DNAs) from karyocytes, (3) examined the IL-6 and TGF-β gene polymorphisms, and (4) analyzed and correlated participants' clinical data with the gene polymorphisms and expressions. The team used a quantitative polymerase chain reaction (qPCR) to examine the expression levels of IL-6 and TGF-β.

Results • Compared to the control group, the disease group: (1) had allele distributions that were significantly different at the rs2069829 locus of the IL-6 gene ($P < .001$) and at the rs3087453 of the TGF-β gene ($P = .004$); (2) had significantly higher frequencies of allele T at the rs2069829 locus of the IL-6 gene and of allele G at the rs3087453 locus of the TGF-β gene; (3) had genotype distributions that were significantly different at the rs2069829 locus ($P < .001$) and the rs2069857 locus ($P = .048$) of the IL-6 gene and at the rs3087453 locus ($P < .001$) of the TGF-β gene; (4) had frequencies that were significantly higher of the TT genotype at the rs2069829 locus, the CC genotype at the rs2069857 locus, and the GC genotype at the rs3087453 locus of the IL-6 gene and the TGF-β gene; (5) had dominant models that were significantly different at the rs2069829 locus of the IL-6 gene ($P = .009$) and at rs3087453 locus of the TGF-β gene ($P = .026$) and had a recessive model that was significantly different at the rs2069857 locus of the IL-6 gene ($P = .040$); (6) had significantly different haplotypes CC ($P < .001$) and TC ($P < .001$) at the rs2069829 locus and the rs2069857 locus of the IL-6 gene and a significantly different haplotype AC ($P = .011$) at the rs1800469 locus and the rs3087453 locus of the TGF-β gene; (7) had an IL-6 gene polymorphism at the rs2069857 locus that was related to the expression of the IL-6 gene ($P < .05$) and an expression of the IL-6 gene for participants with the AA genotype that was significantly lower than for other genotypes; (8) had a TGF-β gene polymorphism at the rs1800469 locus that was associated with the expression of the TGF-β gene ($P < .05$), and an expression for participants with the GG genotype that was significantly higher than for other genotypes; (9) had an IL-6 gene polymorphism at the rs2069857 locus with an overt correlation with the genotype of osteoporotic, thoracolumbar, vertebral compression fracture ($P < .001$). Also, participants in the disease group with the genotype CC mainly had type 2 and 3 fractures, while those with genotype AA primarily had type 0 and 1 fractures.

Conclusions • IL-6 and TGF-β gene polymorphisms and expressions are significantly related to osteoporotic, thoracolumbar, vertebral compression fracture (*Altern Ther Health Med.* 2023;29(3):120-126).

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Osteoporosis is a metabolic disease of the skeletal system, and the onset is mainly associated with patients' age.[1,2] Its main characteristics include microstructural damage of bone tissues; imbalances of components, such as minerals and matrix constituting bones; thinning and brittleness of bones; and increased risk of fracture.[3]

Changes in hormone levels after menopause and endocrinal changes in vivo from aging cause osteoporosis, which can result in the occurrence of osteoporotic, thoracolumbar, vertebral compression fracture.[4-6] This disease is mainly correlated with a reduction in the vertebral bone density and bone quality.[7,8]

The disease's main pathogenesis involves a decrease in the surface density of trabecular bones, which can also influence their morphological structure. Under a certain compressive force, the trabecular bone structure becomes unstable, resulting in local disintegration and fracture.[9] In this process, factors in the body's internal environment such as material balance, immune status, genetic factors, and external environment can all affect the occurrence of osteoporotic, thoracolumbar, vertebral compression fracture.

Therefore, searching for the factors that make an individual susceptible to the disease makes sense to prevent its occurrence. Investigating its pathogeny is of great significance to improving its diagnosis and treatment rates.

Cytokines exert crucial effects in homeostasis modulation and disease development.[10] Multiple cytokines, such as interleukin (IL) and tumor necrosis factor (TGF), cooperate with or antagonize each other to keep a normal physiological state, but their imbalance can cause osteoporotic, thoracolumbar, vertebral compression fracture and jointly affect its development.[11]

Genetic Factors

Two vital cytokines, IL-6 and TGF-beta (TGF-β), play key regulatory roles in cell proliferation, differentiation, aging, and other processes.[12] Some studies have found that IL-6 and TGF-β cytokines can exert key regulatory effects in numerous diseases[13,14] and that the IL-6 and TGF-β genes can influence susceptibility to many diseases, such as systemic lupus erythematosus, in the genetic process.[15] The correlations between IL-6 and TGF-β and osteoporosis are very close.[16,17]

Associations between genes and diseases manifest as the influence of gene expression on disease development as well as the impact of variations in the disease-related genes themselves on the occurrence and development of a disease. Gene polymorphism is a factor that can influence the occurrence of disease, affecting a person's susceptibility to it, and some studies have verified its association with disease.[18,19]

It's important to determine the genetic variations that can lead to compressed fractures of the osteoporotic, thoracic lumbar vertebrae, which would allow medical practitioners to recommend personalized clinical methods to prevent or at least delay development of the disease.

Xiong et al found that the G allele and the GG genotype of the rs1800796 locus of the IL-6 gene may have contributed to increased susceptibility to osteoporotic vertebral compression fracture in Chinese older adults.[20] They also demonstrated that the 572C/G GG genotype of the IL-6 gene may be associated with an increased risk of osteoporosis.[21] In addition, Chen et al found the CT and TT genotypes and the T allele of the rs1982073 locus of the TGF-β gene may contribute to lower susceptibility to osteoporotic vertebral compression fracture.[21]

Current Study

The current study intended to explore the correlations between the gene polymorphisms and gene expressions of the IL-6 and TGF-β genes and osteoporotic, thoracolumbar, vertebral compression fracture.

METHODS

Participants

The research team performed an observational study using data from medical records. The study took place at Xuzhou Medical University in Xuzhou, China. Potential participants were patients with an osteoporotic, thoracolumbar, vertebral compression fracture who had been admitted to the hospital at the university between 2019 and 2021 prior to the study and healthy people who were treated in our department at the same period but were not diagnosed with osteoporotic, thoracolumbar, vertebral compression fracture.

Potential participants in the disease group were included in the study if: (1) they had an osteoporotic, thoracolumbar, vertebral compression fracture; (2) they were aged over 50 years old; (3) they had bone mineral density and bone quality that had decreased as indicated by bone density examination; (4) trauma had not caused their disease; and (5) had abnormal bone metabolism indexes, such as for bone alkaline phosphatase, and had thoracolumbar vertebral fracture that MRI and CT examinations had confirmed.

Potential participants who received treatments in the same department due to other spinal diseases were included in the control group. Those who were diagnosed as osteoporosis examined by Dual-energy X-ray were excluded from the study.

The Ethics Committee of the hospital approved the study's protocols. Signed written informed consents were obtained from the patients and/or guardians.

Procedures

Groups. The research team divided the participants into two groups. The patients became participants in the disease group, and the healthy individuals became participants in the control group.

Data collection. The research team collected participants' demographic and clinical data, such as past medical history and family history. Dr. Tao Zuo was responsible to collect these data via inquiry with the patients.

Sample collection and processing. The research team: (1) collected about 8 mL of peripheral blood from participants, (2) centrifuged it at 3000 rpm for 5 min within 1 h, and

(3) separated the intermediate karyocytes into a new centrifuge tube for the extraction of genomic deoxyribonucleic acids (DNAs).

Genomic DNA extraction. The research team extracted the genomic DNAs using a TIANamp blood genomic extraction kit (TIANGEN, Beijing, China) in strict accordance with the kit's instructions. The team: (1) added protease K (Beyotime, Shanghai, China) to the centrifuge tube according to the sample volume; (2) added the peripheral blood samples; (3) mixed them uniformly using a vortex oscillator (Keygen, Nanjing, China) for one minute; (4) placed the mixture at 65°C for 8 min; (5) added absolute ethyl alcohol to the samples, mixed them well, and transferred them to the adsorption column; (6) added Tris-EDTA buffer solution (Keygen, Nanjing, China) to the adsorption column for centrifugation at 4000 rpm for 1 min; (7) added 200 µL of elution buffer (Keygen, Nanjing, China) to the adsorption column; the solution obtained provided the genomic DNA; (8) conducted the subsequent analysis after the optical density at 260 nm (OD260)/OD280 was 1.8-2.0.

Quantitative polymerase chain reaction (qPCR) amplification and analysis of IL-6 and TGF-β gene polymorphisms. The research team used the qPCR) instrument (Beyotime, Shanghai, China) to amplify the polymorphic regions at the rs2069829 locus and the rs2069857 locus of the IL-6 gene and at the rs1800469 locus and the rs3087453 locus of the TGF-β gene. The total qPCR system of 25 µL contained 0.5 µL of each primer, 1 µL of template DNA, 12.5 µL of Taq enzymes, and 11.5 µL of distilled water (dH_2O. The qPCR conditions were: (1) 95°C for 5 min, (2) (95°C for 30 s, 56°C for 40 s, 72°C for 30 s) × 40 cycles, (3) 72°C for 5 min, and (4) heat preservation at 4°C.

For the IL-6 gene, the primers in each polymorphic region for the rs2069829 locus were forward: "GGCCAGATCCTGTCCAAGC" and reverse: "GTGGGTTTCCACCATTAGCAC", and for the rs2069857 locus were: forward: "CTAATGGTGGAAACCCACAACG" and reverse: "TATCGCCAGGAATTGTTGCTG".

For the TGF-β gene, the primers for the rs1800469 locus were forward: "CAATTCCTGGCGATACCTCAG" and reverse: "GCACAACTCCGGTGACATCAA", and for the rs3087453 locus were forward: "CCACCTGCAAGACCATCGAC" and reverse: "CTGGCGAGCCTTAGTTTGGAC".

The research team sent the qPCR products to Keygen Biotechnology company (Nanjing, China) for sequencing to obtain participants' IL-6 and TGF-β gene polymorphisms through sequencing data analysis.

Detection of IL-6 and TGF-β gene expression. The research team examined the expressions of the IL-6 and TGF-β genes using qPCR. The team used a TRIzol assay (Invitrogen, Carlsbad, CA, USA) to extract total RNAs from the karyocytes in participants' peripheral blood. Following reverse transcription into complementary DNAs (cDNAs), the team examined the expressions of the IL-6 and TGF-β genes using qPCR.

The total reaction system was 25 µL, including 1 µL of upstream and 1 µL of downstream primers, 1 µL of template cDNA, 12.5 µL of 2× Mix, and 25 µL of deionized water. The primer sequences of the IL-6 gene were forward: "CTTCAATACGTCAGACATTCGGG" and reverse: "GTAACCGAATTGTTGCTA". The primer sequences of the TGF-β gene were forward: "CTCCCGTGGCTTCTAGTGC" and reverse: "GCCTTAGTTTGGACAGGATCTG".

Classification of osteoporotic, thoracolumbar, vertebral compression fracture. Using standard, lateral, X-ray images of the whole spinal column, the research team classified the osteoporotic, thoracolumbar, vertebral compression fractures of the disease group into four types using the Genant semiquantitative method[22]: (1) type 0 = a vertebral body with a normal shape and size; (2) type 1 = 20-25% compression in the anterior vertebral body and 10-20% reduction in the projected area of the vertebral body; (3) type 2 = 25-40% compression in the anterior vertebral body and 20-40% reduction in the projected area of the vertebral body; and (4) type 3 = over 40% compression in the anterior vertebral body and more than 40% reduction in the projected area of the vertebral body.

Outcome Measures

The research team: (1) collected peripheral blood from the two groups, (2) extracted genomic deoxyribonucleic acids (DNAs) from karyocytes, (3) examined the IL-6 and TGF-β gene polymorphisms, and (4) analyzed and correlated participants' clinical data with the gene polymorphisms and expressions.

Statistical Analysis

The research team used Statistical Product and Service Solutions (SPSS) 22.0 (IBM, Armonk, NY, USA) for statistical analysis. The team conducted comparisons of measurement data using the t-test and haplotype analysis using the Hardy-Weinberg balance test. In addition, the team used the SHEsis website (http://analysis.bio-x.cn/) for online analysis. $P < .05$ indicated that the difference was statistically significant.

RESULTS

Participants

The study enrolled and analyzed the data of 400 participants, including 200 patients in the disease group and 200 healthy persons in the control group. The disease group included 72 males and 128 females, with an average age of 69.12 ± 8.24 years (data not shown). The control group included 89 males and 111 females, with an average age of 68.23 ± 7.34 years.(data not shown)

Allele Distributions

Table 1 shows the allele distributions at the rs2069829 locus and the rs2069857 locus of the IL-6 gene and at the rs1800469 locus and the rs3087453 locus of the TGF-β gene in the groups. The disease group's allele distributions were significantly different from those of the control group at the

Table 1. Allele Distributions at the rs2069829 Locus and the rs2069857 Locus of the IL-6 Gene and at the rs1800469 Locus and the rs3087453 Locus of the TGF-β Gene

Gene	Locus	Allele	Control Group N=200 N (%)	Disease Group n = 200 n (%)	OR	95% CI	χ^2	*P* value
IL-6	rs2069829	C	103 (51.5)	68 (34.0)	0.47	0.35-0.63	26.47	<.001[a]
		T	97 (48.5)	132 (66.0)				
	rs2069857	C	94 (47.0)	103 (51.5)	0.84	0.63-1.11	1.44	.229
		A	106 (53.0)	97 (48.5)				
TGF-β	rs1800469	A	101 (50.5)	97 (48.5)	0.92	0.69-1.21	0.32	.571
		G	99 (49.5)	103 (51.5)				
	rs3087453	G	89 (44.5)	109 (54.5)	0.66	0.50-0.88	8.01	.004[a]
		C	111 (55.5)	91 (45.5)				

[a]*P* < .05, indicating that the disease group's allele distributions were significantly different from those of the control group at the rs2069829 locus for the IL-6 gene and at the rs3087453 locus for TGF-β gene

Abbreviations: IL-6, interleukin-6; TGF-β, transforming growth factor-beta.

Table 2. Genotype Distributions at the rs2069829 Locus and the rs2069857 Locus of the IL-6 Gene and at the rs1800469 Locus and the rs3087453 Locus of the TGF-β Gene

Gene	Locus	Allele	Control Group n = 200 n (%)	Disease Group n= 200 n (%)	χ^2	*P* value
IL-6	rs2069829	CC	56 (28.0)	33 (16.5)	26.39	<.001[a]
		CT	95 (47.5)	69 (34.5)		
		TT	49 (24.5)	98 (49.0)		
	rs2069857	CC	39 (19.5)	58 (29.0)	5.95	.048[a]
		CA	111(55.5)	90 (45.0)		
		AA	50 (25.0)	52 (26.0)		
TGF-β	rs1800469	AA	53 (26.5)	55 (27.5)	1.73	.419
		AG	97 (48.5)	85 (42.5)		
		GG	50 (25.0)	60 (30.0)		
	rs3087453	GG	38 (19.0)	44 (22.0)	16.98	<.001[a]
		GC	101 (50.5)	129 (64.5)		
		CC	61 (30.5)	27 (13.5)		

[a]*P* < .05, indicating that the disease group's genotype distributions were significantly different from those of the control group at the rs2069829 locus and the rs2069857 locus of the IL-6 gene and at the rs3087453 locus of the TGF-β gene

Abbreviations: IL-6, interleukin-6; TGF-β, transforming growth factor-beta.

rs2069829 locus for the IL-6 gene (*P* < .001) and at the rs3087453 locus for TGF-β gene (*P* = .004). In addition, the disease group had significantly higher frequencies of allele T at the rs2069829 locus for the IL-6 gene and of allele G at the rs3087453 locus for the TGF-β gene.

Genotype Distributions

Table 2 shows the genotype distributions at the rs2069829 locus and the rs2069857 locus of the IL-6 gene and at the rs1800469 locus and the rs3087453 locus of the TGF-β gene in the two groups. The disease group's genotype distributions were significantly different from those of the control group at the rs2069829 locus (*P* < .001) and the rs2069857 locus (*P* = .048) of the IL-6 gene and at the rs3087453 locus of the TGF-β gene (*P* < .001). Moreover, the disease group's frequencies of the TT genotype at the rs2069829 locus, the CC genotype at the rs2069857 locus, and the GC genotype at the rs3087453 locus of the IL-6 gene and the TGF-β gene were significantly higher than those of the control group.

IL-6 Gene Polymorphisms

Table 3 shows the IL-6 gene polymorphisms at the rs2069829 locus and at the rs2069857 locus and the TGF-β gene polymorphisms at the rs1800469 locus and at the rs3087453 locus in the two groups. The disease group's dominant model at the rs2069829 locus of the IL-6 gene (*P* = .009) and at the rs3087453 locus of the TGF-β gene (*P* = .026) and its recessive model at the rs2069857 locus of the IL-6 gene (*P* = .040) was significantly different from those of the control group.

Haplotypes

Table 4 shows the analysis of haplotypes at the rs2069829 locus and the rs2069857 locus of the IL-6 gene and at the rs1800469 locus and the rs3087453 locus of the TGF-β gene in the two groups. The disease group's distributions of the

haplotypes CC ($P < .001$) and TC ($P < .001$) at the rs2069829 locus and the rs2069857 locus of the IL-6 gene and that of the haplotype AC ($P = .011$) at the rs1800469 locus and the rs3087453 locus of the TGF-β gene were significantly different from those of the control group.

Gene Expressions

Figures 1-4 show the correlations between the IL-6 gene polymorphisms at the rs2069829 locus (Figure 1) and at the rs2069857 locus (Figure 2) and the TGF-β gene polymorphisms at the rs1800469 locus (Figure3) and at the rs3087453 locus (Figure 4) and gene expression for the two groups. The IL-6 gene polymorphism at the rs2069857 locus was related to the expression of the IL-6 gene ($P < .05$), and the expression of the IL-6 gene for participants with the AA genotype was significantly lower than for other genotypes. The TGF-β gene polymorphism at the rs1800469 locus was associated with the expression of the TGF-β gene ($P < .05$), and the expression of the TGF-β gene was significantly higher in participants with the GG genotype than for other genotypes.

Correlations of Gene Polymorphisms With Genotypes

Table 5 shows the correlations between the IL-6 gene polymorphisms at the rs2069829 locus and the rs2069857 locus and the TGF-β gene polymorphisms at the rs1800469 locus and the rs3087453 locus and the genotypes for osteoporotic, thoracolumbar, vertebral compression fracture. The IL-6 gene polymorphism at the rs2069857 locus had an overt correlation with the genotype for osteoporotic, thoracolumbar, vertebral compression fracture ($P < .001$). Participants in the disease group with the genotype CC mainly had the type 2 and 3 fractures, while those with the genotype AA primarily had the type 0 and 1 fractures.

Table 3. The IL-6 Gene Polymorphisms at the rs2069829 Locus and the rs2069857 Locus and the TGF-β Gene Polymorphisms at the rs1800469 Locus and the rs3087453 Locus

	Gene	Locus	Allele	Control Group n = 200 n (%)	Disease Group n = 200 n (%)	χ^2	*P* value
Dominant Model	IL-6	rs2069829	CC + CT	151 (75.5)	102 (51.0)	9.34	.009[a]
			TT	49 (24.5)	98 (49.0)		
		rs2069857	CC + CA	150 (75.0)	148 (74.0)	1.44	.487
			AA	50 (25.0)	52 (26.0)		
	TGF-β	rs1800469	AA + AG	150 (75.0)	140 (70.0)	1.05	.592
			GG	50 (25.0)	60 (30.0)		
		rs3087453	GG + GC	139 (69.5)	173 (86.5)	7.33	.026[a]
			CC	61 (30.5)	27 (13.5)		
Recessive Model	IL-6	rs2069829	CC	56 (28.0)	33 (16.5)	5.21	.074
			CT + TT	144 (72.0)	167 (83.5)		
		rs2069857	CC	39 (19.5)	58 (29.0)	6.42	.040[a]
			CA + AA	161 (80.5)	142 (71.0)		
	TGF-β	rs1800469	AA	53 (26.5)	55 (27.5)	1.7	.427
			AG + GG	147 (73.5)	145 (72.5)		
		rs3087453	GG	38 (19.0)	44 (22.0)	3.4	.183
			GG + GC	162 (81.0)	156 (78.0)		

[a]$P < .05$, indicating that the disease group's dominant model at the rs2069829 locus of the IL-6 gene and at the rs3087453 locus of the TGF-β gene and its recessive model at the rs2069857 locus of the IL-6 gene was significantly different from those of the control group.

Abbreviations: IL-6, interleukin-6; TGF-β, transforming growth factor-beta.

Table 4. Haplotype Distributions at rs2069829 and rs2069857 of the IL-6 Gene and at rs1800469 and rs3087453 of the TGF-β Gene (N = 400)

Gene	Haplotype	Control Group n = 200 n (%)	Disease Group n = 200 n (%)	OR	95% CI	χ^2	*P* value
IL-6	CA	52 (26.0)	40 (20.0)	0.723	0.518-1.010	3.641	0.056
	CC	53 (26.5)	28 (14.0)	0.445	0.311-0.638	19.986	<0.001*
	TA	55(27.5)	57 (28.5)	1.051	0.772-1.431	0.1	0.752
	TC	40 (20.0)	75 (37.5)	2.379	1.732-3.270	29.295	<0.001*
TGF-β	AC	59(29.5)	43 (21.5)	0.661	0.479-0.911	6.451	0.011*
	AG	42 (21.0)	54 (27.0)	1.376	0.994-1.904	3.704	0.054
	GC	53 (26.5)	49 (24.5)	0.891	0.648-1.227	0.499	0.480
	GG	46 (23.0)	54 (27.0)	1.249	0.906-1.722	1.853	0.174

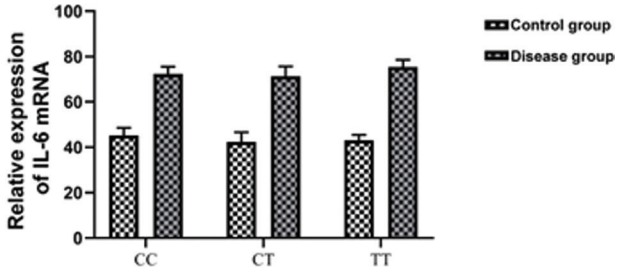
*$P < .05$, indicating that the disease group's distributions of the haplotypes CC and TC at the rs2069829 locus and the rs2069857 locus of the IL-6 gene and that of the haplotype AC at the rs1800469 locus and the rs3087453 locus of the TGF-β gene were significantly different from those of the control group.

Abbreviations: IL-6, interleukin-6; TGF-β, transforming growth factor-beta.

DISCUSSION

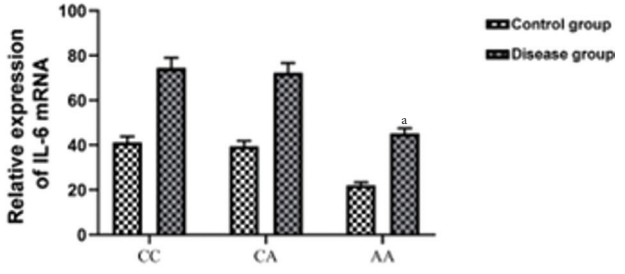
The present study screened site polymorphisms e of IL-6 and TGF-β genes and finally chose IL-6 gene rs2069829, rs2069857, TGF-β gene rs180046 and rs3087453 as the study's targets. The study's findings indicate that IL-6 and TGF-β gene polymorphisms are related to the onset of osteoporotic, thoracolumbar, vertebral compression fracture, which is a core susceptible factor for the disease, and medical

Figure 1. Relationship Between the IL-6 Gene Polymorphism at the rs2069829 Locus and its Expression (N = 400)



Abbreviations: IL-6, interleukin-6.

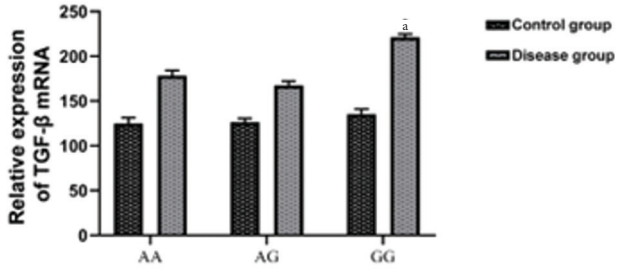
Figure 2. Relationship Between the IL-6 Gene Polymorphism at the rs2069857 Locus and its Expression



[a]*P* < .05, indicating that the IL-6 gene polymorphism at the rs2069857 locus was related to the expression of the IL-6 gene and that the expression of the IL-6 gene for participants with the AA genotype was significantly lower

Abbreviations: IL-6, interleukin-6.

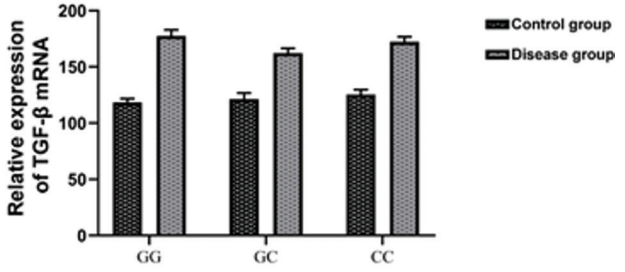
Figure 3. Relationship Between the TGF-β Gene Polymorphism at the rs1800469 Locus and its Expression



[a]*P* < .05, indicating that the TGF-β gene polymorphism at the rs1800469 locus was associated with the expression of the TGF-β gene and that the expression of the TGF-β gene was significantly higher in participants with the GG genotype

Abbreviations: TGF-β, transforming growth factor-beta.

Figure 4. Relationship Between the TGF-β Gene Polymorphism at the rs3087453 Locus and its Expression



Abbreviations: TGF-β, transforming growth factor-beta.

Table 5. Correlations of the IL-6 gene polymorphisms at the rs2069829 Locus and the rs2069857 Locus and the TGF-β Gene Polymorphisms at the rs1800469 Locus and the rs3087453 Locus With the Genotypes of Osteoporotic Thoracolumbar Vertebral Compression Fracture

Gene	Locus	Genotype	n (%)	Genotype 0 n (%)	Genotype 1 n (%)	Genotype 2 n (%)	Genotype 3 n (%)	*P* value
IL-6	rs2069829	CC	33 (16.5)	6 (18.2)	12 (36.3)	9 (27.3)	6 (18.2)	.581
		CT	69 (34.5)	13 (18.8)	24 (34.9)	23 (33.3)	9 (13.0)	
		TT	98 (49.0)	25 (25.5)	21 (21.4)	33 (33.7)	19 (19.4)	
	rs2069857	CC	58 (29.0)	1 (1.7)	12 (20.7)	18 (31.0)	27 (46.6)	<.001[a]
		CA	90 (45.0)	11 (12.2)	30 (33.3)	44 (48.9)	5 (5.6)	
		AA	52 (26.0)	32 (61.5)	15 (28.8)	3 (5.8)	2 (3.9)	
TGF-β	rs1800469	AA	55 (27.5)	10 (18.2)	15 (27.3)	20 (36.3)	10 (18.2)	.124
		AG	85 (42.5)	18 (21.2)	24 (28.2)	29 (34.1)	14 (16.5)	
		GG	60 (30.0)	16 (26.7)	18 (30.0)	16 (26.7)	10 (16.6)	
	rs3087453	GG	44 (22.0)	15 (34.0)	8 (18.2)	16 (36.4)	5 (11.4)	.071
		GC	129 (64.5)	14 (10.9)	46 (35.6)	44 (34.1)	25 (19.4)	
		CC	27 (13.5)	15 (55.6)	3 (11.1)	5 (18.5)	4 (14.8)	

[a]*P* < .05, indicating that the IL-6 gene polymorphism for the rs2069857 locus had an overt correlation with the genotype for osteoporotic, thoracolumbar, vertebral compression fracture

Abbreviations: IL-6, interleukin-6; TGF-β, transforming growth factor-beta.

practitioners can used them as screening indicators for the disease.

The current study also found that the disease group's dominant model at the rs2069829 locus of the IL-6 gene ($P = .009$) and at the rs3087453 locus of the TGF-β gene ($P = .026$) and its recessive model at the rs2069857 locus of the IL-6 gene ($P = .040$) were different from those of the control group. In addition, its distributions of haplotypes CC ($P < .001$) and TC ($P < .001$) at the rs2069829 locus and the rs2069857 locus of the IL-6 gene and those of haplotype AC ($P = .011$) at the rs1800469 locus and the rs3087453 locus of the TGF-β gene were different from those of the control group. It can be inferred that the effects of IL-6 and TGF-β gene polymorphisms on the pathogenesis of osteoporotic, thoracolumbar, vertebral compression fracture may be complex and multifactorial, so the area is worthy of further research.

The expressions of IL-6 and TGF-β genes may directly influence the occurrence and development of osteoporotic, thoracolumbar, vertebral compression fracture. The detection of the associations of IL-6 and TGF-β gene polymorphisms with their expressions illustrated that the IL-6 gene polymorphism at the rs2069857 locus was related to its expression ($P < .05$), which was notably lower in patients with the AA genotype. The TGF-β gene polymorphism at the rs1800469 locus was associated with its expression ($P < .05$), and TGF-β gene expression was significantly higher in patients with GG genotype. The above results suggest that IL-6 and TGF-β gene polymorphisms can affect gene expressions, which may be a crucial mechanism of the gene polymorphisms that affect disease onset and progression.

Finally, based on the analysis of clinical data, the current found that the IL-6 gene polymorphism at the rs2069857 locus had an overt correlation with the genotype of osteoporotic, thoracolumbar, vertebral compression fracture ($P < .001$). Patients with genotype CC mainly had type 2 and 3 fracture, while those with genotype AA primarily had type 0 and 1 fracture.

The main limitation of this study was that the sample was from a single medical centre. Thus, to confirm the role of L-6 and TGF-β gene polymorphisms in patients with osteoporotic, thoracolumbar, vertebral compression fracture, a multi-center study with larger sample size is required.

CONCLUSIONS

The IL-6 gene polymorphism has an overt association with the progression of osteoporotic, thoracolumbar, vertebral compression fracture, and patients with different genotypes may have different progression rates of the disease. The polymorphism is a good indicator for the monitoring of disease progression.

AUTHORS' DISCLOSURE STATEMENT

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