

# Serum Apolipoprotein B/apolipoprotein A1 Ratio in Relation to Intervertebral Disc Herniation : A Cross-sectional Frequency-Matched Case-Control Study

## Fei Chen

Department of Cardiovascular, Pingxiang people's hospital, Pingxiang 337000, Jiangxi Province, P. R. China.

## Tongde Wu

Department of Spinal Surgery, Shanghai East Hospital, Tongji University School of Medicine, 150 JiMo Road, Shanghai 200120, China.

## Song Guo

Department of Orthopedics, Shanghai General Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai 200080, P. R. China.

## Junwen Huang

Department of Cardiovascular, Pingxiang people's hospital, Pingxiang 337000, Jiangxi Province, P. R. China.

## Qiang Fu

Department of Orthopedics, Shanghai General Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai 200080, P. R. China.

## Yaqing pan

Department of Spinal Surgery, Shanghai East Hospital, Tongji University School of Medicine, 150 JiMo Road, Shanghai 200120, China.

## Huiying Zhang

Department of Spinal Surgery, Shanghai East Hospital, Tongji University School of Medicine, 150 JiMo Road, Shanghai 200120, China.

## Desheng Wu

Department of Spinal Surgery, Shanghai East Hospital, Tongji University School of Medicine, 150 JiMo Road, Shanghai 200120, China.

## Qi Chen

Department of Cardiovascular, the Second Affiliated Hospital of Nanchang University, Nanchang 330000, Jiangxi Province, P. R. China.

## Iijun Li

Department of Spinal Surgery, Shanghai East Hospital, Tongji University School of Medicine, 150 JiMo Road, Shanghai 200120, China.

Xinhua Li (✉ [xinhuali1013@163.com](mailto:xinhuali1013@163.com))

## Research

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# Abstract

## Background

In recent decades, the serum lipid profile of apolipoprotein(a) (Lp(a)) level and apolipoprotein B/apolipoprotein A1 ratio (Apo B/ApoA1) ratio were found more representative for serum lipid level and were recognized as the independent risk factors for various diseases. Although the serum lipid levels of total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C) were found associated with symptomatic IDH, no studies have been conducted to date for the evaluation of the association of Apo AI, Apo B, Lp(a) and Apo B/Apo AI levels with symptomatic IDH.

## Materials

A total of 1,839 Chinese patients were recruited in the present study. 918 patients were diagnosed as IDH cases and were enrolled in the experimental group. A control group of 921 patients underwent a physical examination during the same period. The serum lipid levels of TC, TG, LDL-C, HDL-C, Lp(a), Apo B and Apo B/Apo AI were examined and analyzed.

## Results

The patients in the control group were collected randomly from patients who were matched with the baseline levels of the aforementioned lipid molecular. The patients with IDH exhibited significantly higher TC, TG, LDL, Apo B and Lp(a) levels compared with the control subjects. The percentage of high-TC, high-TG, high-LDL, high-Apo B and high-Lp(a) were significantly higher in the IDH group. However, hyperlipidaemia was not associated with the degenerated segment of the IDH ( $P=0.201$ ). The odds ratios (OR) for the incidence of IDH with an elevated LDL-C, TC, TG, Lp(a), Apo B and Apo B/Apo AI were 1.583, 1.74, 1.62, 1.58, 1.49 and 1.39, respectively. The correlation analysis revealed the correlation between elevated LDL-C, TC, TG, Apo B, Lp(a) and incidence of IDH was significant ( $R^2_{LDL}=0.017$ ;  $R^2_{TC}=0.004$ ;  $R^2_{TG}=0.015$ ;  $R^2_{Apo B}=0.004$ ;  $R^2_{LP(a)}=0.021$ ) ( $P<0.05$ ).

## Conclusions

The present study suggests that elevated levels of serum TC, TG, LDL, Apo B, Lp(a) and Apo B/Apo AI are associated with a higher risk for IDH.

## Background

Intervertebral disc degeneration (IVDD) and related diseases are a leading cause of disability, notably job-related disability[1-3]. Despite the extensive investigation of the etiology and treatment of IVDD, the underlying pathophysiological mechanisms remain unclear[3-8]. A variety of risk factors, such as excessive mechanical overload, aging, tissue injury, smoking, abnormal metabolism levels, and genetic

risk have been found to contribute to the onset and progression[9-11]. Among these factors, abnormal lipid metabolism and atherosclerosis (AS) have been implicated in the development of symptomatic intervertebral disc herniation (IDH) and/or low back pain[12-16]. A Finnish study performed by Leino-Arjas et al[12] identified that the positive correlation between higher total cholesterol (TC), low density lipoprotein cholesterol (LDL-C), triglycerides (TG) levels and sciatica. Several studies further demonstrated that triglycerides (TG) and total cholesterol (TC) were associated with the severity of low back pain and symptomatic IDH[13-18].

With the increased research on serum lipid, the lipoprotein fraction of apolipoprotein A1 (Apo A1) and apolipoprotein B (Apo B) and the ratios of apolipoprotein B/apolipoprotein A1 (Apo B/Apo A1), and apolipoprotein(a) (Lp(a)) have received considerable attention in the investigation of dyslipidaemia related diseases in recent years, and Apo B/Apo A1 and Lp(a) were recognized as the independent risk factors for various diseases, including osteoarthritis and AS[19-21]. However, the possible association between Apo A1, Apo B, Lp(a) and symptomatic IDH remains undiscovered.

In this study, a frequency-matched case-control study of serum lipid levels obtained from patients with symptomatic IDH was conducted in order to evaluate the relationship between serum lipid levels and symptomatic IDH in our study. We found that the patients with IDH exhibited significantly higher TC, TG, LDL, Apo B and Lp(a) levels compared with the control subjects. The percentage of high-TC, high-TG, high-LDL, high-Apo B and high-Lp(a) were significantly higher in the IDH group. Moreover, the odds ratios (OR) analysis revealed elevated LDL-C, TC, TG, Lp(a), Apo B and Apo B/Apo A1 had a higher risk of IDH incidence. The correlative analysis further suggested elevated LDL-C, TC, TG, Lp(a), Apo B and Apo B/Apo A1 are significantly closely with incidence of IDH. Our findings revealed that elevated levels of serum TC, TG, LDL, Apo B, Lp(a) and Apo B/Apo A1 are associated with a higher risk for IDH.

## Methods

All procedures described in the present study were approved by the Ethics Committee of our institution. All patients provided written informed consent. The detailed primary flow-charts were presented in Figure 1. A total of 4,349 patients accepted the MRI scan and were potentially considered for inclusion from 2010 to 2019 in our institution. A total of 3,431 patients were excluded due to failure to meet the inclusion criteria (history of spinal disorders (n=155), multiple IDHs(n=367), spondylolysis(n=98), foraminal or central canal stenosis (n=187), spinal trauma (n=67), primary osteoarthritis of the operated and/or contralateral joint (n=367), inflammatory joint disease (n=211), diabetes (n=311), coronary heart disease (n=516), cerebrovascular disease (n=217), hypertension (n=467), smoking(n=468)). A total of 918 patients (399 men and 519 women; mean age: 60.74±12.69 years, range 18 to 93years) met our inclusion criteria and were enrolled in our study in group 1 (symptomatic IDH group). A total of 921 patients (control group) (401 men and 520 women; mean age: 61.02±12.59 years, range 18-91years), who underwent physical examination and conducted the MRI scan during the same period, were matched with the baseline of the symptomatic IDH group (Table 1). The patients in the control group were excluded for IVDD by the MRI[22, 23]. The procedure of selecting the patients in these two groups and giving the

diagnosis were performed by experienced spine surgeons who did not know the purpose of the study. No statistically significant differences in the variables age, gender, labor intensity and BMI were noted between the two groups ( $P>0.05$ ). The work has been reported in line with the STROCSS criteria[24].

## **Patient Selection**

Patients in group 1 were included in the study if they had (a) symptomatic cervical spondylotic myelopathy, the thoracic and lumbar IDH. The diagnosis of cervical spondylotic myelopathy and of thoracic and lumbar IDH was conducted on the basis of clinical presentation, physical examination, radiography, electromyography, computerized tomography (CT) and/or MRI. (b) Absence of symptom relief despite adequate medical treatment.

The inclusion criteria for group 2 were the following: (1) The patients who underwent physical examination in the same period and were excluded for IVDD by spine MRI from 2009 to 2019[2]. The patients who were frequency-matched by age and gender with the patients of Group 1 (Table1).

The exclusion criteria for groups 1 and 2 were the following: history of spinal disorders, multiple IDHs, spondylolysis, spondylolisthesis, foraminal or central canal stenosis, spinal trauma, spondyloarthritis, primary osteoarthritis of the operated and/or contralateral joint, inflammatory joint disease, diabetes, coronary heart disease, cerebrovascular disease, hypertension, smoking and age lower than 18 years[16].

## **The definition of symptomatic IDH**

### **The cervical disc herniation [25]**

(1)Typical sensory radicular symptoms (pain or paresthesias) were always present. (2)Motor (weakness and atrophy), sensory (hypesthesia or dysesthesia), and reflex (diminution or absence of tendon reflexes) symptoms, if present, were confined to 1 dermatome and/or myotome that corresponded to pain and/or paresthesias; Positive signs: a positive Spurling's test, Eaten test and Hoffman sign. (3)Clinical symptoms and signs correlated with the level of root compression as a result of disc herniation and/or spondylotic lateral stenosis.

### **The thoracic disc herniation [26]**

(1)Localized axial back pain and/or axial back pain with radiation into the lumbar spine; sensory impairment; (2) Special nerve root irritation signs: the pain can even mimic cardiac disease and/or present as abdominal and/or shoulder pain; (3) Neurologic deficit: paraparesis and monoparesis; spasticity and hyperreflexia; bladder dysfunction; (knee jerk or ankle reflex).

### **The lumbar disc herniation [16]**

(1)Low back pain with unilateral or bilateral lower limb radicular pain; (2)Special nerve root irritation signs: straight leg raising test and strengthen test and/or femoral stretch test depending on the level of

injury (3) Neurologic deficit: muscle weakness, numbness, and/or lack of the corresponding reflex (knee jerk or ankle reflex).

### **Imaging diagnosis**

All the patients enrolled in the present study underwent the spine examination by 1.5T MRI. Both T2 and T1-weighted images were combined and used to assess the IVDD from C1/2 to L5/S1 regions by an experienced spine surgeon who was blinded to the study. The degree of IVDD on MRI was based on the Pfirrmann grade system[25]. The criteria for grade 1 are the following: Its structure is homogeneous and bright white in color; The distinction of nucleus and anulus is clear; The signal intensity for the disc is hyperintense and isointense compared with the cerebrospinal fluid; The height of the intervertebral disc is normal. The criteria for grade 2 are the following: Its structure is nonhomogeneous in the absence and/or presence of horizontal bands; The distinction of the nucleus and anulus is clear; The signal intensity for the disc is hyperintense and isointense compared with the cerebrospinal fluid; The height of the intervertebral disc is normal. The criteria for grade 3 are as follows: Its structure is progressing to nonhomogeneous and gray in color; The distinction of nucleus and anulus is unclear; The signal intensity for the disc is intermediate; The height of the intervertebral disc is normal to slightly decreased. The criteria for grade 4 are the following: Its structure is progressing to nonhomogeneous and gray to black in color; The distinction of the nucleus and the anulus is lost; The signal intensity for the disc is intermediate to hypo-intense; The height of the intervertebral disc is normal to slightly decreased. The criteria for grade 5 are as follows: Its structure is progressing to nonhomogeneous and black in color; The distinction of the nucleus and anulus is lost; The signal intensity for the disc is hypointense; The disc space is collapsed[27-29].

### **Blood examination**

All blood samples were collected in an identical manner between 07.30 and 08.30 a.m. following an overnight fast that started at 12.00 midnight. Biochemical analyses of blood samples were conducted on fresh specimens. Fasting blood samples were collected, and five milliliters of each sample was centrifuged at 4,000 rpm for 6 min. The serum was extracted from the samples, and the concentrations of TC, TG, LDL-C, HDL-C, Apo A1, Apo B, Lp(a) were measured by an automatic biochemical analyser in an identical manner. The normal levels of the following indexes exhibited the following range TC from 0 to 5.2 mmol/L; TG from 0 to 1.7 mmol/L; LDL-C from 0 to 3.4 mmol/L; HDL-C from 0.7 to 2.0 mmol/L; ApoEA1 from 1 to 1.6 g/L; Lp(a) from 0 to 30 mg/mL; Apo B from 0.6 to 1.1 g/L. The normal value of the ratio of Apo B/Apo A1 was 0.87 for the male subjects, and 0.65 for the female subjects[30].

### **Statistical analysis**

Continuous variables were expressed as the mean  $\pm$  standard deviation (SD) and analyzed with unpaired t-tests. Categorical variables were expressed as a percentage of the number and analyzed with a chi-square test. The normality analysis was carried out for the continuous variables. SPSS (Version 20.0) was used for all statistical analyses. A P value that was lower than 0.05 was regarded as statistically

significant. Multivariate logistic regression was used to evaluate the effects of serum lipids on symptomatic IDH. The effect indicators were odds ratio (OR) and 95 % confidence interval (CI). The data of continuous variables in the present study followed an ordinary normal distribution. The adjustment for multiple comparisons was conducted in the present study. A P value that was lower than 0.007 ( $P < 0.007$ ) was considered statistically significant following the adjustment for multiple comparisons (Table 1 and Figure 2). The correlations analysis was carried out in the present study. A P value that was lower than 0.05 ( $P < 0.05$ ) was considered statistically significant, A P value that was lower than 0.01 ( $P < 0.01$ ) was considered extremely statistically significant.

## Results

### **IDH patients exhibited significantly higher TC, TG, LDL, Apo B, Lp(a) and Apo B/Apo AI levels**

The serum concentrations of TC, TG, LDL-C, HDL-C, Apo AI, Apo B and Lp(a) were measured in all patients (Figure 2). In Group 1 (IDH), the concentration levels of TG, total TC, LDL-C, HDL-C, Apo B and Lp(a) were  $1.63 \pm 1.26$  mmol/L,  $4.50 \pm 1.48$  mmol/L,  $2.67 \pm 0.9$  mmol/L,  $1.16 \pm 0.29$  mmol/L,  $0.80 \pm 0.22$  g/L and  $25.35 \pm 24.01$  mg/dl, respectively. In Group 2 (control group), the concentration levels of TC, TG, LDL-C, HDL-C, Apo AI, Apo B and Lp(a) were  $4.23 \pm 2.18$  mmol/L,  $1.4 \pm 0.91$  mmol/L,  $2.52 \pm 0.83$  mmol/L,  $1.21 \pm 0.36$  mmol/L,  $0.76 \pm 0.23$  g/L and  $22.45 \pm 21.11$  mg/dl, respectively. The patients with symptomatic IDH indicated significantly higher levels of TG ( $P = 0.002$ ), TC ( $P = 0.00$ ), LDL-C ( $P = 0.00$ ), Apo B ( $P = 0.00$ ), Lp(a) ( $P = 0.006$ ). No statistically significant differences were noted for the HDL-C ( $P = 0.125$ ) and Apo AI ( $P = 0.326$ ). The ratios of Apo B/Apo AI were higher in the symptomatic IDH comparing with control group ( $0.78 \pm 0.33$  versus  $0.71 \pm 0.25$ ,  $P < 0.01$ ).

### **The percentage of high-TC, high-TG, high-LDL, high-Apo B and high-Lp(a) were significantly increased in the IDH group**

The percentage of dyslipidemia incidence in the control and IDH group were further investigated in our study. The incidence of the high TC, high TG, high-LDL-C, low-HDL-C, Apo AI, Apo B and Lp(a) were 31.19%, 13.85%, 20.17%, 7.52%, 14.9%, 30.8% and 28.9%, respectively, compared to 23.33%, 15.34%, 14.8%, 5.98%, 13.6%, 21.76% and 51.4% that was noted in the control group, respectively (Table 3). The incidence of the high-TC, high-TG and high-LDL-C, Apo B and Lp(a) were significantly higher in the IDH group compared with the control group ( $P = 0.000$ ,  $P = 0.00$ ,  $P = 0.02$ ,  $P = 0.000$ ,  $P = 0.000$  respectively). No statistically significant differences were noted with regard to HDL-C ( $P = 0.189$ ) and Apo AI ( $P = 0.412$ ).

### **The association between serum lipid abnormalities and the degree of IVDD**

To further investigate correlation for the incidence of a symptomatic IDH with an elevated LDL-C, TC, TG, Lp(a), Apo B and Apo B/Apo AI, the correlation analysis was conducted between serum lipid abnormalities and the degree of IVDD (Pfarrmann grade). As shown in Figure 3, the correlation between elevated LDL-C, TC, TG, Apo B, Lp(a) and incidence of IDH were significant ( $R^2_{LDL} = 0.017$ ,  $P < 0.001$ ;  $R^2_{TC} = 0.004$ ,  $P < 0.004$ ;  $R^2_{TG} = 0.015$ ,  $P < 0.001$ ;  $R^2_{Apo B} = 0.004$ ,  $P < 0.001$ ;  $R^2_{LP(a)} = 0.021$ ,  $P < 0.008$ ). These

results suggested that patients with higher LDL-C, TC, TG, Lp(a), Apo B and Apo B/Apo AI levels are closely related with disc herniation.

### **Hyperlipidaemia did not affect the degenerated segment of the intervertebral disc**

The categorical data of the patients with disc herniation were analyzed in order to examine the associations between hyperlipidaemia and the disc segment in the intervertebral disc group. The hyperlipidaemia group (n=689) exhibited the following percentages of degenerated segments in the cervical, thoracic and lumbar regions: 13.9%, 1.3% and 84.8%, respectively. In contrast to the hyperlipidemic samples, the normal serum lipids group exhibited incidences of 18.8%, 1.3% and 79.9% that corresponded to the cervical, thoracic and lumbar regions, respectively (n=229). No significant differences in the herniation segments were noted between these two groups ( $p = 0.201$ ) (Figure 4).

The categorical data were further analyzed in order to identify the association between the serum lipid levels and the segment of disc herniation in the cervical and lumbar regions. Considering the small sample of affected segment in the thoracic disc herniation, we only analyzed the serum lipid levels and segment of disc herniation in the cervical and lumbar regions.

The values of the total segment in the cervical, thoracic and lumbar regions were 137, 12 and 769 respectively. No significant differences were noted between serum lipid levels in the C3-C4 ( $P=0.282$ ) and C5-6 ( $P=0.373$ ) segments with regard to TC levels (Figure 5A). Similarly, no significant differences were observed in the C3-C4 ( $P= 0.108$ ) and C5-6 segments with regard to LDL-C levels ( $P=0.254$ ) (Figure 5C). With regard to the levels of Apo B, the C5-6 segment in the hyperlipidaemia group (31.9%) was higher than that of the normal group (24.2%), although no significant differences were noted (Figure 5D,  $P=0.2$ ). With regard to the levels of ApoA (Figure 5E), Lp(a) (Figure 5F) and triglycerides (TG) (Figure 5B), the distribution herniation segment in the hyperlipidaemia and control groups exhibited similar trends both in the lumbar and cervical segments. However, we do not get the significance statistic in our study. Comparing with cervical and lumbar IDH, the incident of thoracic IDH is quite low. The relatively small sample size in our study may contribute to the no-significance result.

### **Patients with elevated LDL-C, TC, TG, Lp(a), Apo B and Apo B/Apo AI levels exhibited a higher risk of disc herniation**

To further identify risk for the incidence of a symptomatic IDH with an elevated LDL-C, TC, TG, Lp(a), Apo B and Apo B/Apo AI, multivariate logistic regression analysis was performed. As shown in Table 4, the odds ratios (ORs) for the incidence of a symptomatic IDH with an elevated LDL-C, TC, TG, Lp(a), Apo B and Apo B/Apo AI were 1.583 (CI, 1.427-1.796), 1.74(CI, 1.282-2.365), 1.62 (CI, 1.295-2.023), 1.58(CI, 1.255-1.975) , 1.49 (CI, 1.346-1.661) and 1.39(CI, 1.254-1.595), respectively ( $P<0.01$ ). These results suggested that patients with higher LDL-C, TC, TG, Lp(a), Apo B and Apo B/Apo AI levels exhibited a higher risk of disc herniation.

## **Discussion**

The association between serum lipid and IVDD related disease has been examined by a multitude of studies[12-16]. Elevated levels of TC, LDL-C and TG have been shown to be associated with sciatica[12], back pain and/or disc herniation[13-16, 28]. In agreement with these results, our data showed IDH patients exhibited significantly higher TC, TG, LDL levels and the percentage of high-TC, high-TG, high-LDL were significantly increased in the IDH group.

Results from several clinical prospective studies indicate that the Apo B/ApoA1 ratio is a simple, accurate risk factor for cardiovascular, osteoarthritis, rheumatoid arthritis, metabolic syndrome disease[19-21, 27]. A Swedish prospective study showed that the Apo B/ApoA1 was a robust and specific marker in predicting the risk of coronary disease and ischemic events[19]. Recently, more and more study found that the Apo B/ApoA1 ratio is the independent risk factor among smoking, hypertension, abdominal obesity, diabetes, psychosocial stress, and acute myocardial infarction [20, 21, 27, 31, 32]. However, as aged related degenerated disease, whether any association between Apo AI, Apo B, Apo B/Apo AI and Lp(a) levels and symptomatic IDH are still unclear.

In the present study, the relationship between Apo AI, Apo B, Lp(a) and symptomatic IDH were examined for the first time. As a result, the levels of Apo B and Lp(a) were shown to positively associate with the incidence of symptomatic IDH. Apo B serves as an essential structural component of chylomicrons, VLDL, intermediate density lipoprotein (IDL) and LDL-C. For the LDL-C, Apo B is a ligand that facilitates cholesterol delivery to the tissues and promotes cholesterol accumulation in the arterial tissue. However, Apo AI is a structural component of HDL-C that facilitates the uptake of cholesterol from the peripheral cells. Moreover, Apo AI is an activator of the lecithin-cholesterol acyltransferase, a key enzyme helping transport of cholesterol to the liver for digesting. Thus, the plasma concentration levels of these Apo B/Apo AI may reflect cholesterol transport ability to the peripheral tissues and indicate a balance between atherogenic and anti-atherogenic factors[31, 32]. Elevated levels of the plasma concentrations of Apo B and increased proportion of the Apo B/Apo AI ratio were observed in symptomatic IDH patients suggested a prominent cholesterol transport to the peripheral tissues including IVD in these patients. Lp(a) is composed of a lipoprotein particle, having the similar protein and lipid proportion with LDL-C. Various studies have shown that high levels of Lp(a) in plasma can be a risk factor for cardiovascular disease, osteoarthritis, and rheumatoid arthritis[33]. The plasma concentrations of Lp(a) are associated with a genetic basis and race/ethnicity [34]. At the same time, the plasma Lp(a) levels may be affected by age, drugs, diabetes, diet and so on. In the present study, it was shown that the level of Lp(a) was increased in the intervertebral disc herniation group. The current study is the first study to report this finding in the field of symptomatic intervertebral disc herniation.

The precise pathophysiologic mechanism underlying the connection between serum lipid levels and lumbar disc herniation remains unclear. The increasing levels of TC, TG, LDL-C, Apo B and Lp(a) in IDH patients could be mainly caused by several reasons. Firstly, the IVD is a poorly vascularized region, whose nutritional supply is through the blood capillary penetration of endplate cartilage and the annual fibrosis[29]. High levels of serum cholesterol[28], triglycerides [28, 35-37], LDL-C[38], Apo B and Lp(a) are considered contribute to atherosclerosis. The presence of atherosclerotic will inhibit the vascular supply

to the poorly vascularized IVD and induced IVDD/IDH[39]. In agreement with our hypothesis, the association between symptomatic IDH and atherosclerosis were identified by a lot of studies. A study that included 86 people concluded that atherosclerosis in the abdominal aorta and notably stenosis of the ostia of segmental arteries may play a vital role in symptomatic IDH[40]. Another 25-year follow-up study showed the calcific atherosclerotic deposits in the posterior wall of the abdominal aorta increased the risk of disc herniation and back pain[41]. Secondly, the activated inflammatory cells induced by high serum lipid levels may comprise an important pathway in the development of symptomatic IDH for hyperlipidaemia patients. The activation of cytokines plays a significant role in the development of IVDD/IDH[39, 42]. Previous studies have reported that pro-inflammatory cytokines were closely associated with serum lipid levels[5, 43]. Therefore, the increased serum lipid levels may enhance the inflammatory response and/or the basic level of systemic inflammation, which can in turn contribute to disc herniation[6]. Thirdly, the oxidized low-density lipoprotein (oxLDL) and the increased expression of lectin-like oxidized low-density lipoprotein receptor 1 (LOX-1) that are caused by dyslipidaemia may also be involved in the development of symptomatic IDH. Our previous study suggested[44] that the levels of the oxLDL and LOX-1 were positively correlated with the extent of IDH. The mechanism of action involved the increase in the expression of MMP3 that was induced by LOX-1. This in turn caused the oxLDL to significantly reduce the viability of human nucleus pulpous. The production of oxLDL usually originates from LDL-C that is oxidized under oxidative stress conditions. Therefore, the elevated LDL-C levels can increase level of oxLDL/LOX-1 and accelerate IVDD.

As is known, elevated levels of TC, TG, LDL-C, Apo B, Lp(a) and reduced HDL-C level are atherogenic lipid marker. The management of cardiovascular disease has traditionally focused on reducing serum lipid levels[45], In this study, we found that elevated serum lipid levels were significantly correlated with IDH and High serum lipid levels predicted a higher incidence of IDH. This association opens the way for a new approach to reducing the risk of IDH/IVDD disease by controlling serum lipid levels.

There were several limitations in the present study: Firstly, no data were provided regarding the levels of very low-density lipoproteins (VLDL). Secondly, this was a retrospective case-control study, thus the causal relationships between serum lipid components and symptomatic IDH remain unclear. These associations can only be ascertained by a follow-up study that will examine the incidence and/or progression rates of symptomatic IDH cases of the same cohort. In the current study, we do not determine whether elevated lipid levels directly give rise to IDH/IVDD, or the elevation of lipids causes other disorders, which in turn lead to IDH/IVDD. In order to prove cause and effect relationships and to find effective treatments for IVDD, a large longitudinal follow-up observations and intervention studies is needed[16]. In the following investigations, we will enlarge the sample size to illustrate the potential association between serum lipids and disc herniation.

## Conclusion

The level of TC, TG, LDL-C, Apo B (Apo B/Apo AI) and Lp (a) were positively correlated with the incidence of symptomatic IDH. However, hyperlipidaemia did not affect the degenerated segment of the

intervertebral disc. This association provides novel evidence regarding the reduction of the risk of symptomatic IDH disease by the control of the serum lipid levels.

## Declarations

**Ethical Approval and consent to participate:** All procedures performed in studies involving human participants were approved prospectively by the authors' human subjects Institutional Review Board.

**Informed consent** All of the participants consented to participate in this study.

## Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

## Consent for publication

Not applicable

## Competing interests

The authors declare that they have no competing interests

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## Author contributions

XL and FC interpreted the data and wrote the initial draft of the manuscript. XL, TW, SG, JH, QF, YP, HZ, DW, and LJ conceived, supervised the study, and wrote the manuscript. QC and LL provided critical suggestions during the study. All authors read and approved the final manuscript.

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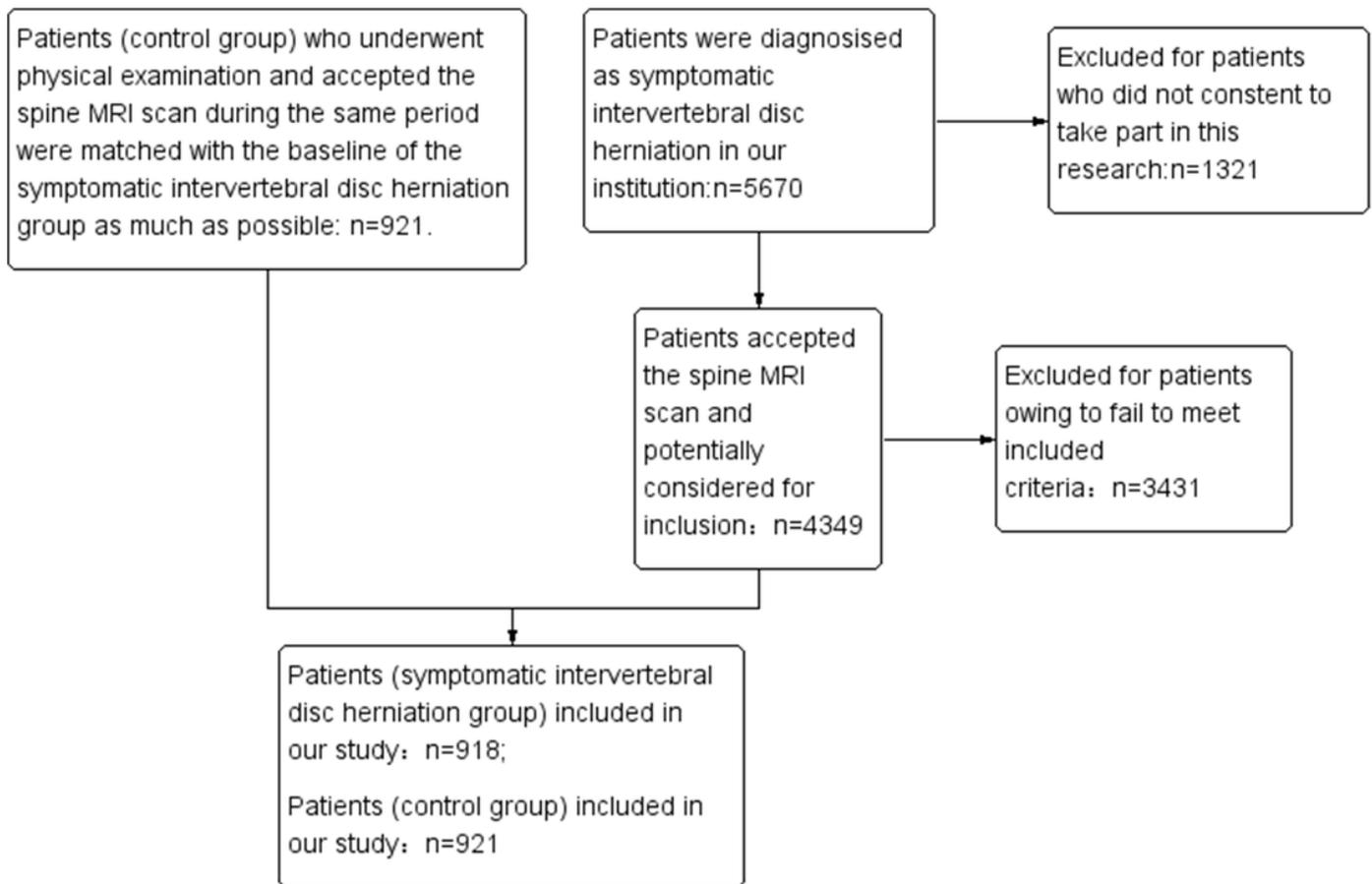
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## Tables

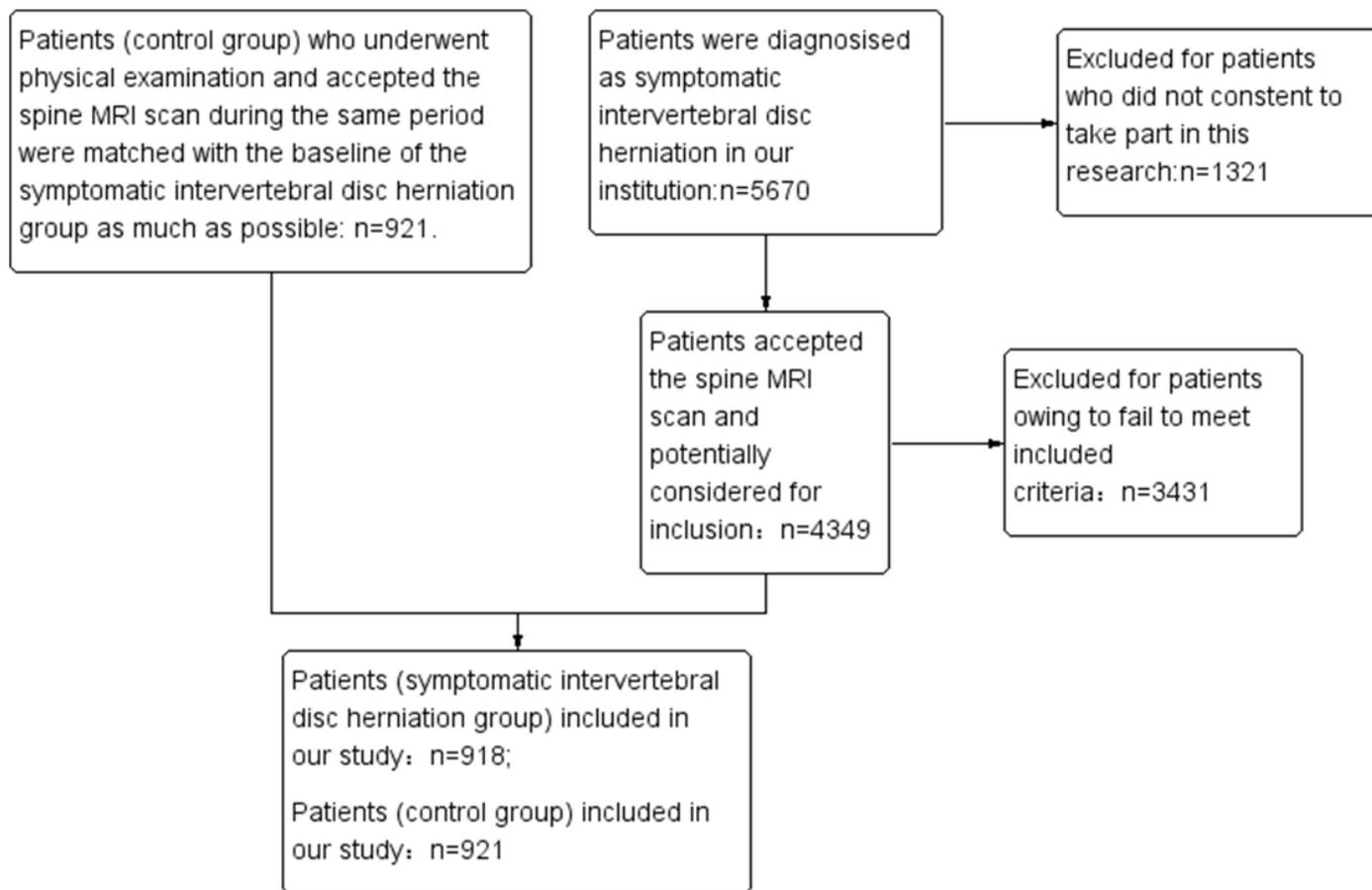
Due to technical limitations, table 1, 2, 3 and 4 is only available as a download in the Supplemental Files section.

## Figures



**Figure 1**

The flow-chart of including and excluding



**Figure 1**

The flow-chart of including and excluding

- Control group
- Symptomatic intervertebral disc herniation group

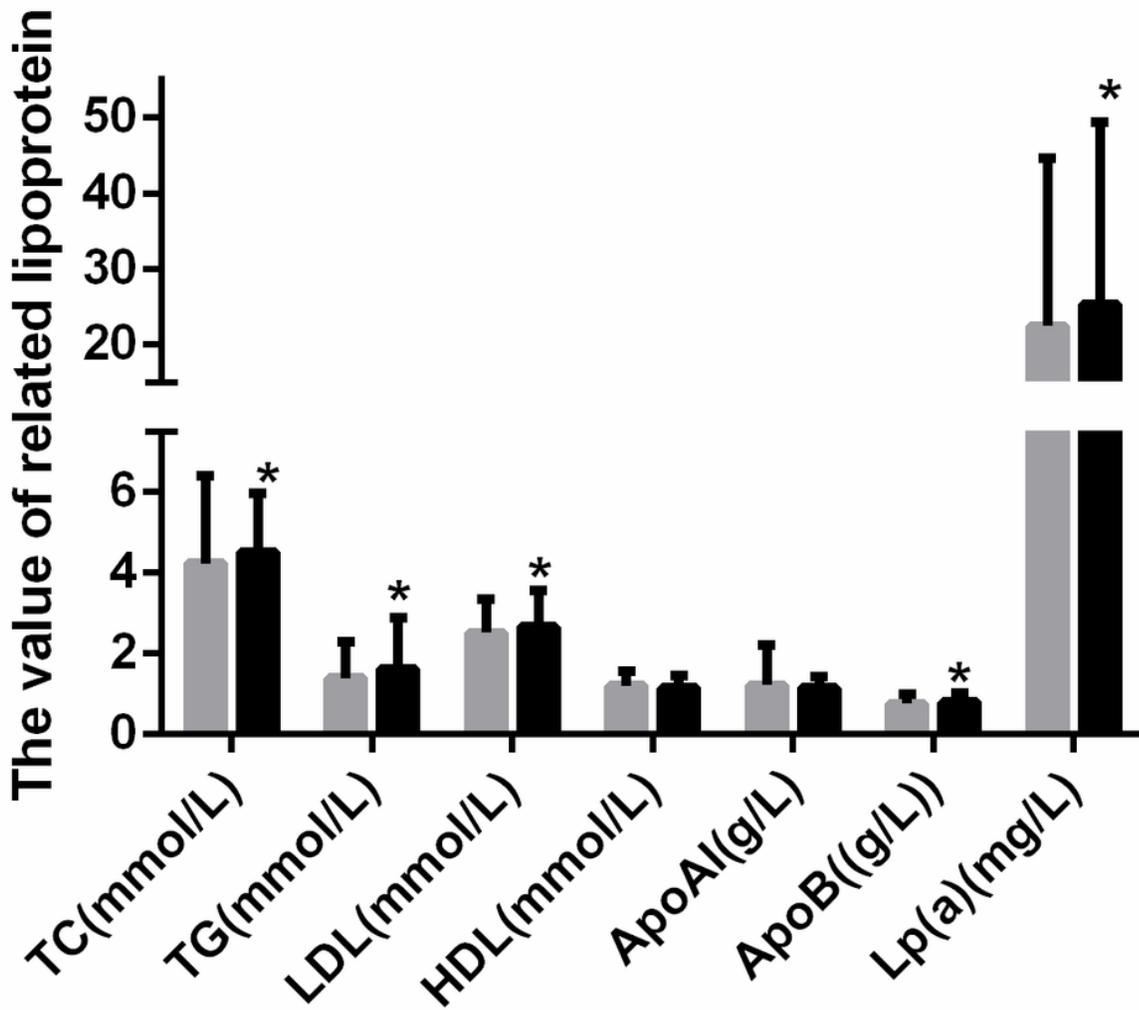


Figure 2

IDH patients exhibited significantly higher TC, TG, LDL, Apo B, Lp(a) and Apo B/Apo AI levels All data are reported as the mean ± s.d. Statistical significance was determined by one-way ANOVA and Student's t-test. \*P < .05. NS = not statistically significant.

- Control group
- Symptomatic intervertebral disc herniation group

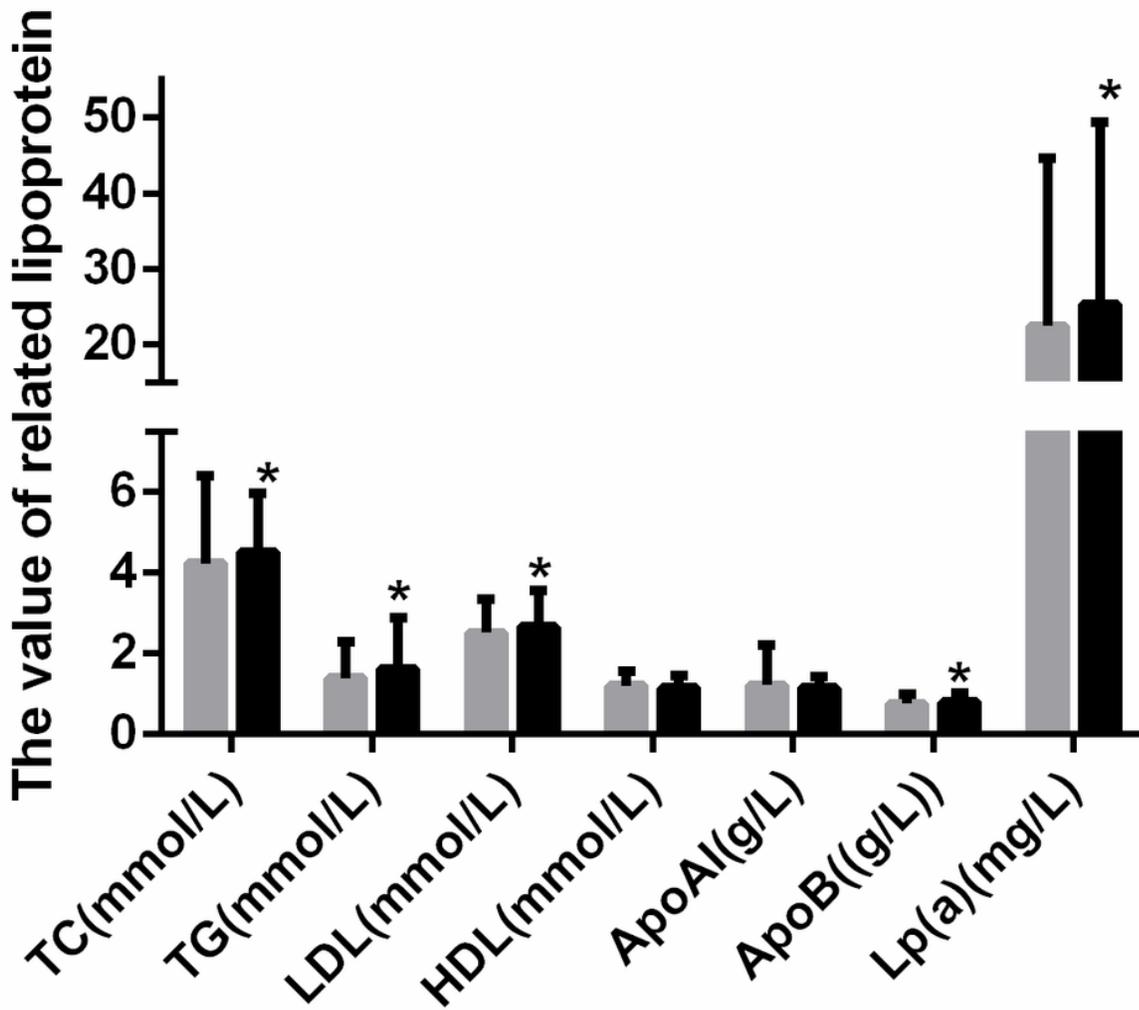
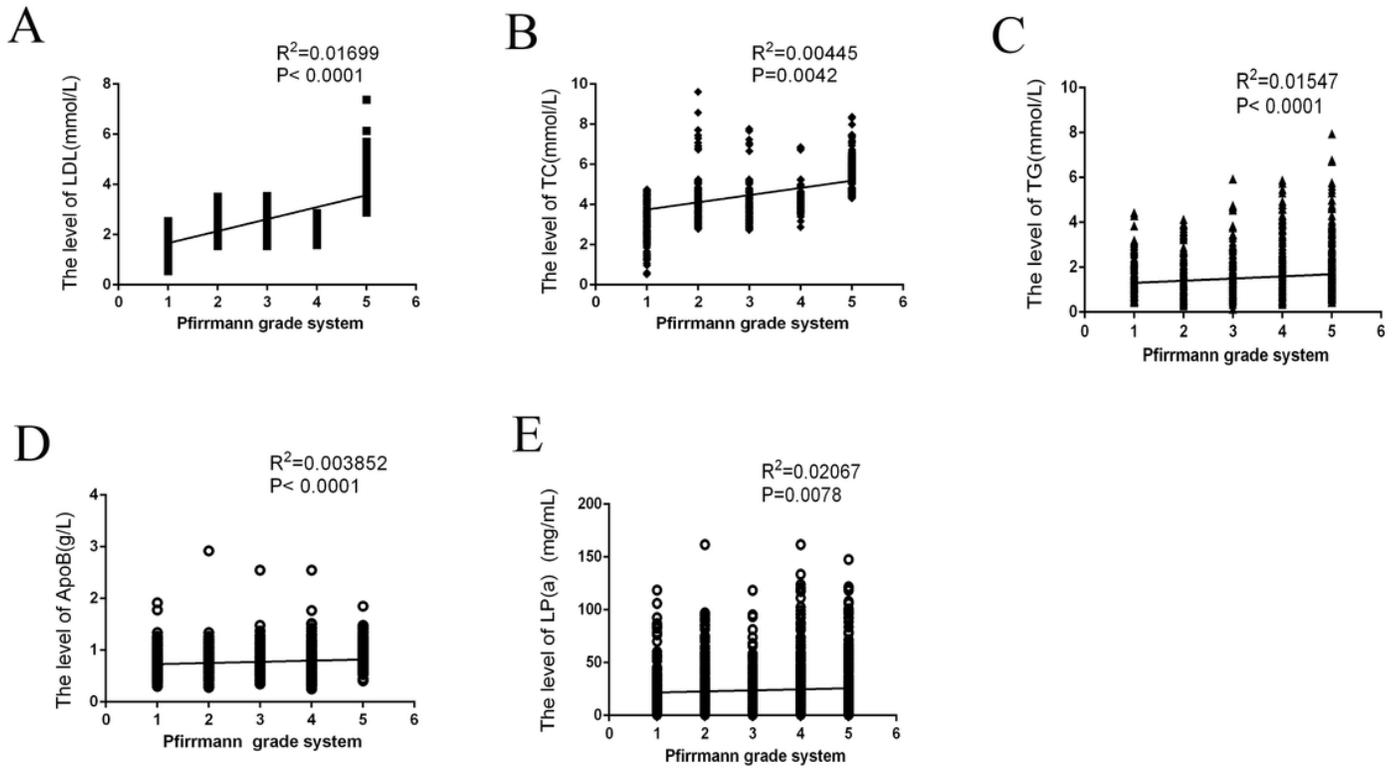


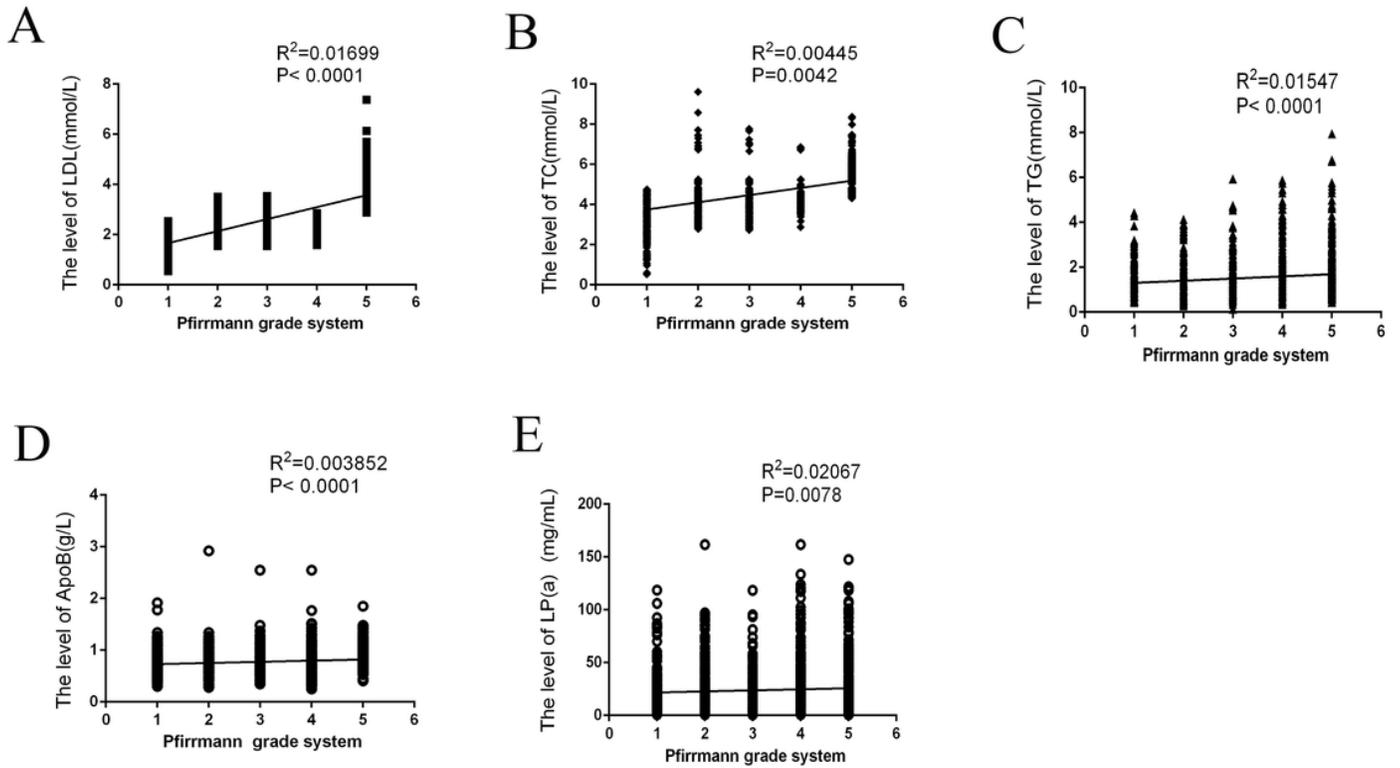
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**Figure 3**

The association between serum lipid abnormalities and the grade of IVDD The correlation analysis between serum LDL (A), TC (B), TG (C), Apo B (D), LP(a) (E) and the grade of IVDD evaluated by pfirsman grade system.



**Figure 3**

The association between serum lipid abnormalities and the grade of IVDD. The correlation analysis between serum LDL (A), TC (B), TG (C), Apo B (D), LP(a) (E) and the grade of IVDD evaluated by pfirrmann grade system.

### The relationship between lipidaemia and affected segment

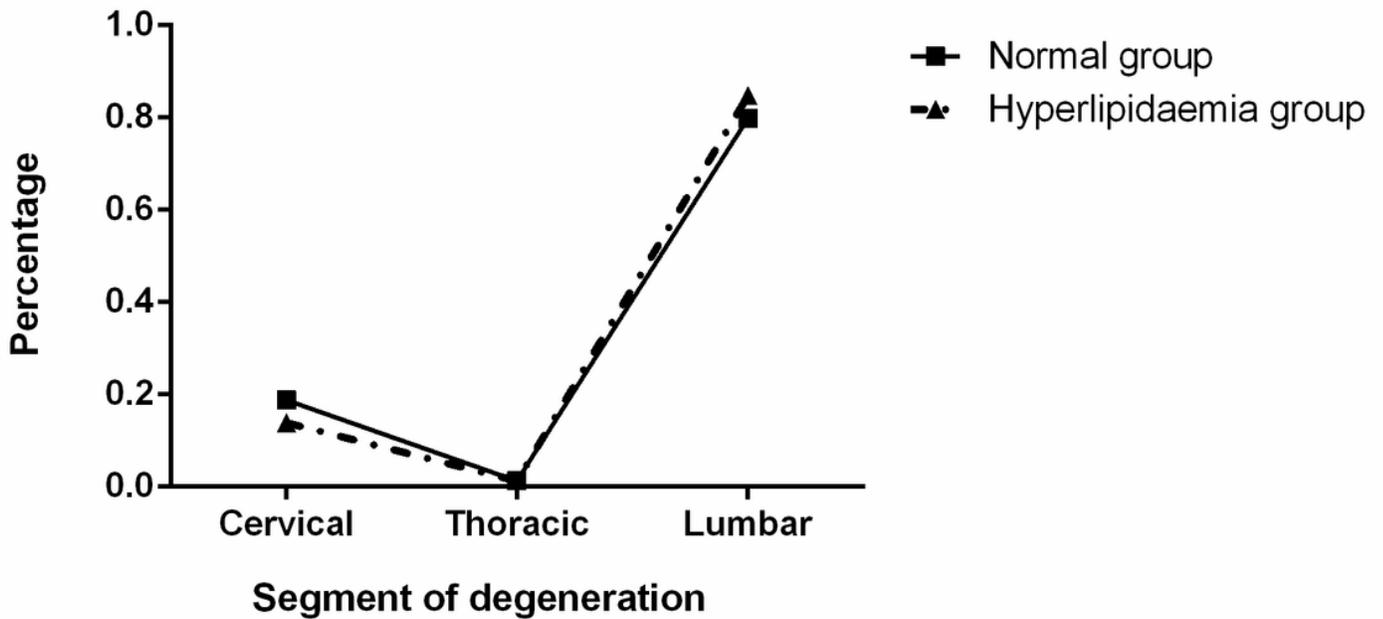


Figure 4

Hyperlipidaemia did not affect the segment of degenerated intervertebral disc

### The relationship between lipidaemia and affected segment

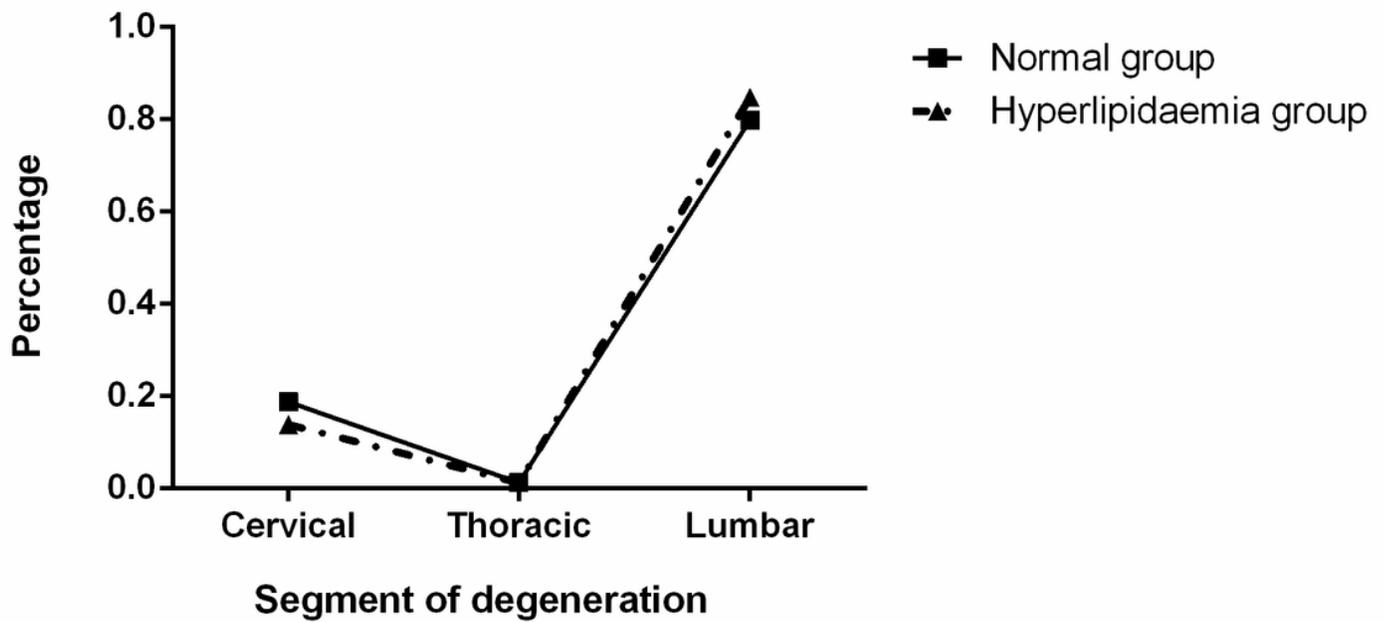
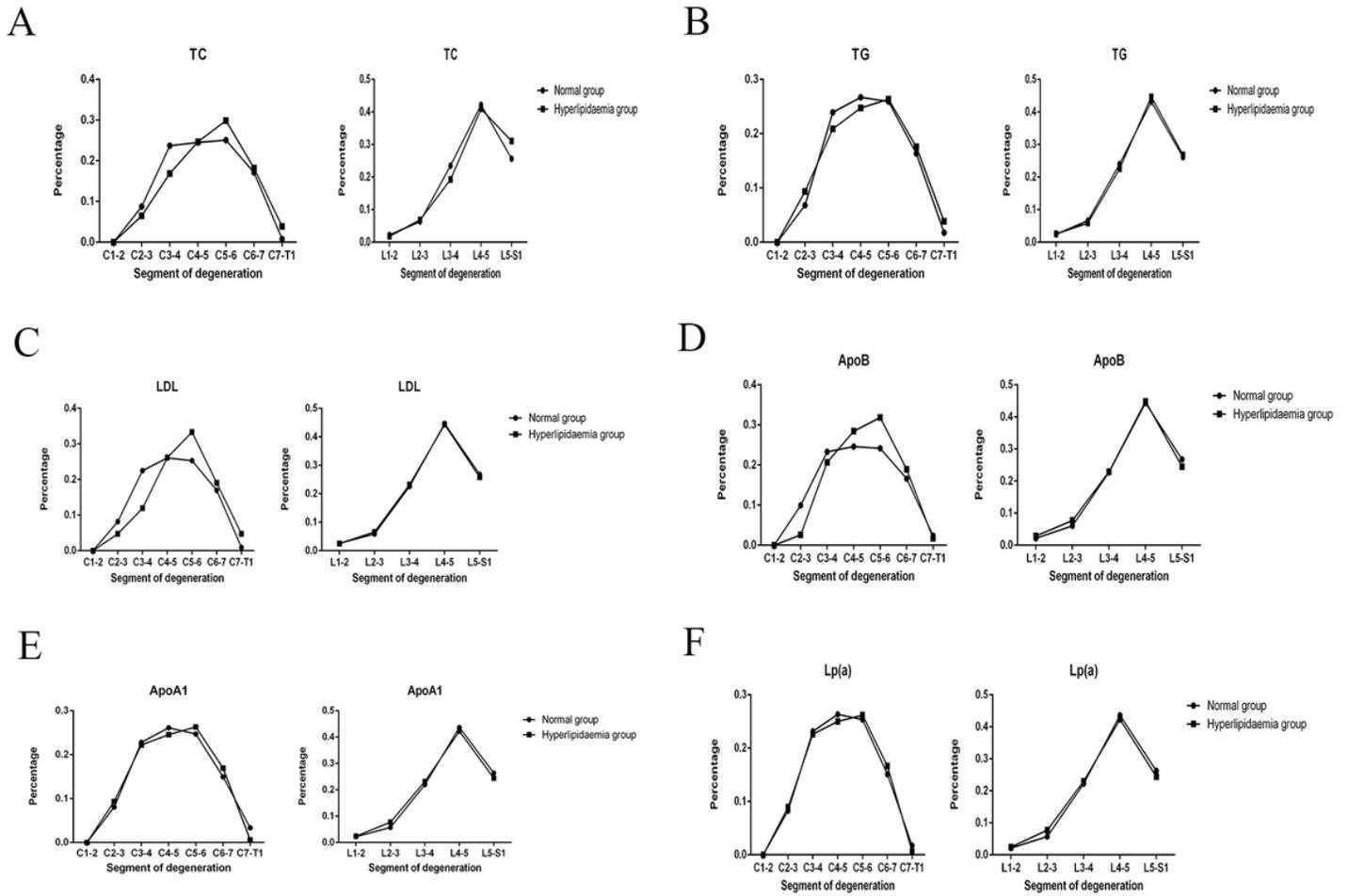


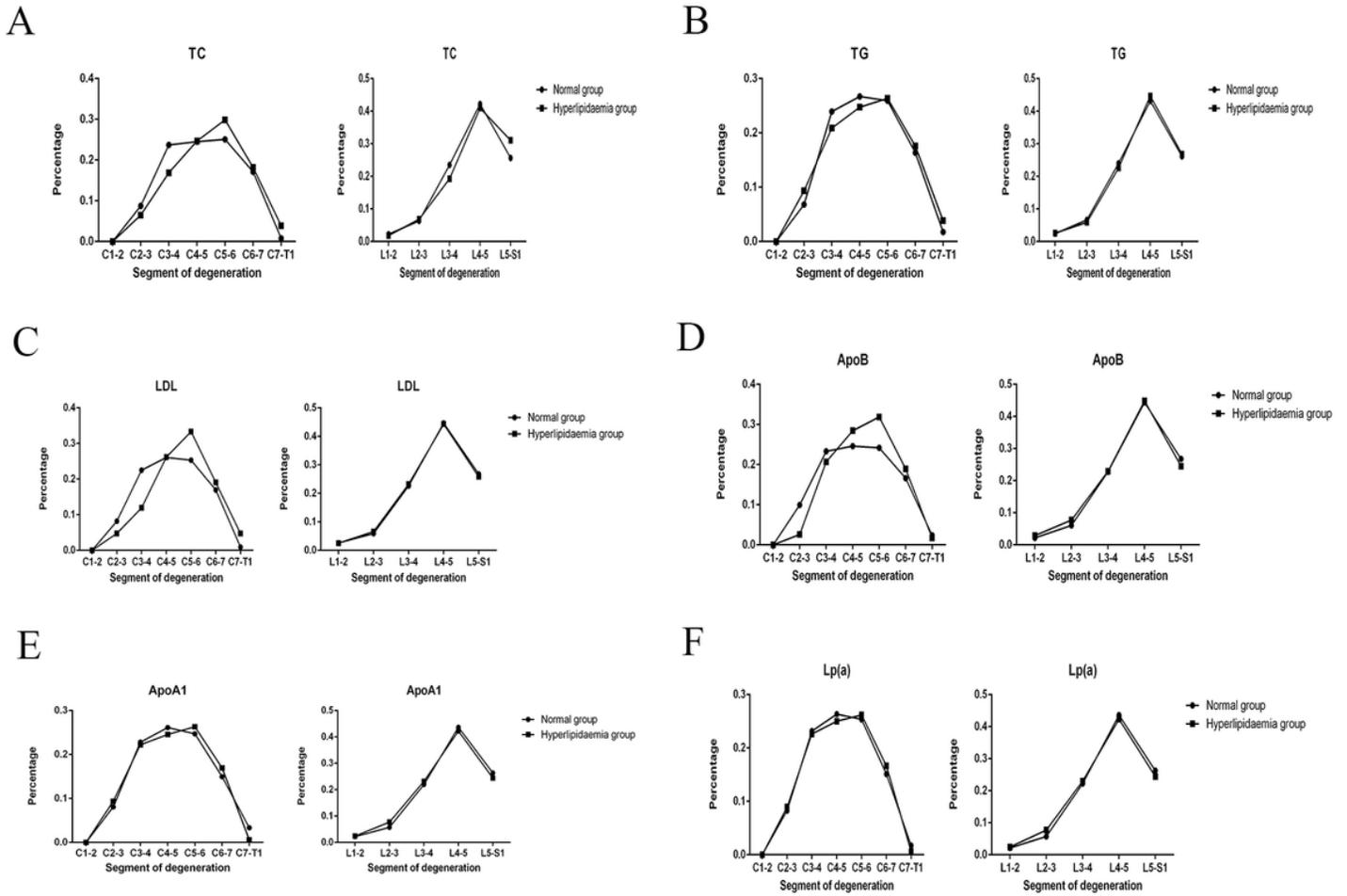
Figure 4

Hyperlipidaemia did not affect the segment of degenerated intervertebral disc



**Figure 5**

Hyperlipidaemia did not affect the incidence of intervertebral disc degenerated segment in cervical and lumbar spine. The percentage of degenerated segment in spine with High TC (A); TG (B); LDL-C (C); Apo B (D); Apo AI (E); Apolipoprotein (F) group.



**Figure 5**

Hyperlipidaemia did not affect the incidence of intervertebral disc degenerated segment in cervical and lumbar spine. The percentage of degenerated segment in spine with High TC (A); TG (B); LDL-C (C); Apo B (D); Apo A1 (E); Apolipoprotein (F) group.

## Supplementary Files

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