

Does High Blood Pressure Have an Effect on Intervertebral Fibrocartilage Histology?

Erhan ŞAHİN^{1*}, Damla Gül FINDIK², Özlem TÜRELİK³

¹: Bilecik Seyh Edebali University, Faculty of Medicine, Histology and Embryology Department, Bilecik, Türkiye

²: Bilecik Seyh Edebali University, Faculty of Medicine, Histology and Embryology Department, Bilecik, Türkiye

³: Bilecik Seyh Edebali University, Faculty of Medicine, Pathology Department, Bilecik, Türkiye

Erhan SAHIN ORCID No: 0000-0003-2152-0542

Damla Gul FINDIK ORCID No: 0000-0001-8028-627X

Ozlem TURELIK ORCID No: 0000-0001-6057-9171

*Corresponding author: erhansahinn@gmail.com

(Received: 13.02.2025, Accepted: 04.03.2025, Online Publication: 26.03.2025)

Keywords

Fibrocartilage,
Intervertebral disc,
High blood pressure,
Histopathology,
Histomorphometry

Abstract: Since the cartilage tissue is fed by the vessels in the surrounding connective tissue, it is a very difficult tissue to repair. Therefore, cardiovascular diseases primarily affect the cartilage tissue. In this study, the possible effects of high blood pressure on discus intervertebralis were examined histopathologically and histomorphometrically. Discus intervertebralis of 13 normotensive and 13 hypertensive patients were compared histopathologically and histomorphometrically. Demographic information of the patients was obtained from the patient registration system of the hospital. Hematoxylin-eosin stained slices were used for histopathological evaluation. In histological sections, chondrocytes and lacunae diameters were measured at 400x magnification in 10 different areas with a computer morphometric measurement program. Discus intervertebralis of normotensive and hypertensive patients did not differ in terms of chondrocyte count and lacunae diameter. The mean age of hypertensive patients (61.69±13.55) was higher than the mean age of normotensive patients (42±8.84) (p<0.05). The gender ratio of the groups did not show a statistical difference (p>0.05). In this study, it was shown that the discus intervertebralis of normotensive and hypertensive patients who underwent lumbar discectomy were not different in terms of histopathologically and histomorphometrically (in terms of chondrocyte number and lacunae diameter).

Yüksek Tansiyonun Omurlar Arası Fibröz Kıkırdak Histolojisi Üzerinde Etkisi Var Mıdır?

Anahtar Kelimeler

Fibrokartilaj,
Omurlar arası disk,
Yüksek tansiyon,
Histopatoloji,
Histomorfometri

Öz: Kıkırdak doku, çevresindeki bağ dokusunda bulunan damarlarla beslendiğinden onarımı çok zor bir dokudur. Bu nedenle kardiyovasküler hastalıklar öncelikle kıkırdak dokusunu etkiler. Bu çalışmada, yüksek tansiyonun discus intervertebralis üzerindeki olası etkileri histopatolojik ve histomorfometrik olarak incelenmiştir. 13 normotansif ve 13 hipertansif hastanın discus intervertebralis'i histopatolojik ve histomorfometrik olarak karşılaştırılmıştır. Hastaların demografik bilgileri hastanenin hasta kayıt sisteminden elde edilmiştir. Histopatolojik değerlendirme için hematoksilin-eozin boyalı kesitler kullanılmıştır. Histolojik kesitlerde, kondrosit ve lakün çapları, morfometrik ölçüm programı ile 10 farklı alanda 400x büyütmede ölçülmüştür. Normotansif ve hipertansif hastaların discus intervertebralis'i kondrosit sayısı ve lakün çapı açısından farklılık göstermemiştir. Hipertansif hastaların yaş ortalaması (61.69±13.55), normotansif hastaların yaş ortalamasından (42±8.84) yüksekti (p<0.05). Grupların cinsiyet oranı istatistiksel olarak fark göstermedi (p>0.05). Bu çalışmada lomber disektomi uygulanan normotansif ve hipertansif hastaların discus intervertebralislerinin histopatolojik ve histomorfometrik (kondrosit sayısı ve lakün çapı) olarak farklı olmadığı gösterildi.

1. INTRODUCTION

Intervertebral discs (ID) are located between our vertebrae. In intervertebral discs, the outer structure, which we call annulus fibrosus, surrounds the nucleus pulposus structure in the center. While the annulus fibrosus is in the structure of fibrous cartilage, the nucleus pulposus consists of a gel-like substance. Fibrous cartilage is a tissue with few chondrocytes and abundant matrix. The extracellular matrix contains abundant type I collagen, chondroitin sulfate and dermatan sulfate. Nucleus pulposus is a gel-like matrix containing abundant hyaluronic acid. Since there is no perichondrium in the cartilage tissue of the ID, their nutrition is provided by the capillaries in the subchondral plate of vertebrae and the surrounding connective tissue [1, 2]. Vascular support of the ID is very important in this respect.

Lumbar disc herniation is an ID pathology that significantly reduces the quality of life of patients. The herniated nucleus pulposus compresses the nerve root and causes inflammation in that area. Its treatment has an important place in the country's health expenditures. Depending on the condition of the pathology, treatment methods such as physiotherapy, rest, lifestyle changes, analgesic and antispasmodic agents are applied first. The latest surgical methods are used [3]. As in many diseases, cardiovascular causes come to the fore in cartilage injuries. Ischemia-induced osteoarthritis is a good example [4]. There are studies in the literature showing that arterial hypertension is directly related to joint osteoarthritis [5, 6].

Hypertension is defined as a condition in which arterial blood pressure is above normal values. In other words, it is the condition that the blood pressure is higher than 140 mm/Hg in systole and 90 mm/Hg in diastole. Hypertension is a chronic disease whose prevalence is increasing day by day both in our country and in the world. Hypertension is the etiology of many diseases, especially cardiovascular diseases. Considering the diseases that affect human and public health, it is a disease that is relatively easy to treat compared to others [7].

In this study, the IDs of patients with high arterial blood pressure and those with normal arterial blood pressure who have undergone lumbar disc herniation surgery will be compared histopathologically and histomorphometrically.

2. MATERIAL AND METHOD

2.1. Experimental Design

This study is a retrospective study. Tissues of patients who had undergone lumbar disc herniation surgery without any metabolic disease were used as the control group. Tissues of patients who were hypertensive and had lumbar disc herniation surgery (blood pressure higher than 140 mm/Hg in systole, 90 mm/Hg in diastole) were used for the experimental group.

2.2. Ethical Statements

The study was carried out in compliance with the Declaration of Helsinki with the approval of Bilecik Seyh Edebali University, Faculty of Medicine, Non-Invasive Clinical Research Ethics Committee, dated 27.12.2022 and numbered 8-2.

2.3. Study Population, Inclusion and Exclusion Criteria for Samples

26 patients who underwent lumbar discectomy at Bilecik Training and Research Hospital between January 2022 and June 2023 were included in the study. Age and gender parameters were also reported for demographic analysis. Patients with possible independent external factors such as cervical discectomy, hypo/hyperthyroidism and diabetes mellitus were excluded.

2.4. Histopathological and Histomorphometric Evaluation

After the tissues were surgically removed, they were immediately placed in 10% neutral buffered formaldehyde for fixation. Tissues were embedded in paraffin after dehydration, clearing and paraffin impregnation. Sections of 5 μ m thickness were taken from paraffin blocks to slides. Slides were kept in the oven for deparaffinization. Then, the slides were passed through xylol and decreasing ethyl alcohol series (100%, 90%, 80%, and 70%) respectively. After the slides were stained with hematoxylin & eosin stain, they were passed through increasing series of ethyl alcohol (70%, 80%, 90% and 100%). Slides were kept in xylol for 30 minutes and then mounted with entellan. Tissues were examined and photographed under a microscope (Olympus CX23) with an Olympus camera (Olympus EP50). The groups were first evaluated histopathologically by a pathologist. Chondrocytes were counted in 10 different fields of slides at 400 \times magnification [8]. In addition, lacunae diameters were measured in counted chondrocytes.

2.5. Statistical Analysis

Statistical package program was used for statistical analysis. Continuous variables were checked for normality using the Kolmogorov-Smirnov test. Student's t-test was used to compare parametric data. Chi-square test was used for the analysis of categorical data. A p-value below 0.05 was considered statistically significant.

3. RESULTS

3.1. Histopathologic Results

Normotensive and hypertensive sections had histopathologically similar appearance (Figure 1).

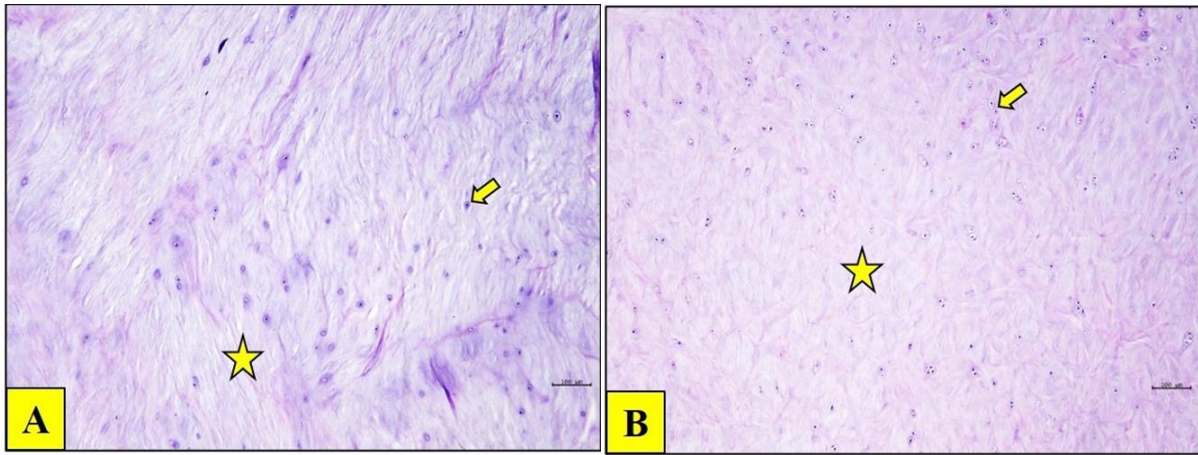


Figure 1. Hematoxylin-eosin staining of discus intervertebralis from normotensive (A) and hypertensive (B) patients. Normotensive and hypertensive sections had similar chondrocyte (yellow arrow) and extracellular matrix (yellow star) histology. In image A and B, the bars are 100µm.

3.2. Comparison of Chondrocyte Morphology in Normotensive and Hypertensive Patients

The mean chondrocyte count per field at x400 magnification of the groups was 3.22±0.77 in normotensive patients and 3.15±0.75 in hypertensive

patients. The mean lacunae diameters were measured as 13.05±0.47 in normotensives and 13.53±1.41 in hypertensives. There was no significant difference between the groups in terms of chondrocyte count and lacunae diameter (p>0.05) (Figure 2).

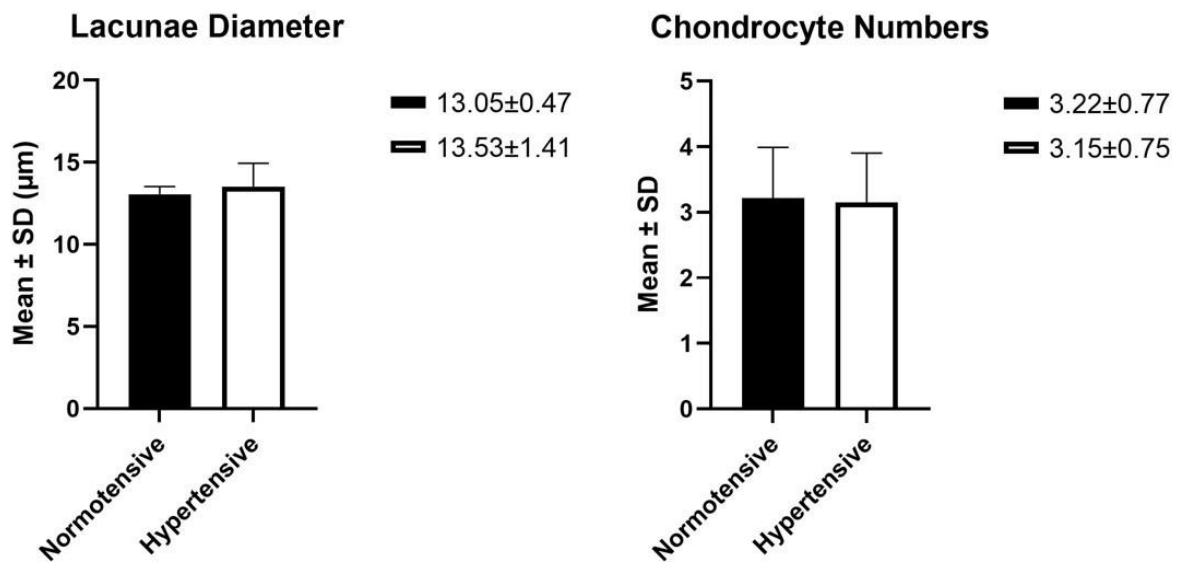


Figure 2. The mean chondrocyte numbers and lacunae diameter in normotensive and hypertensive patients. Student’s t-test, p>0,05.

3.3. Demographic Characteristics of Normotensive and Hypertensive Patients

In the study population, the mean age of hypertensive patients (61.69±13.55) was higher than the mean age of normotensive patients (42±8.84) (p<0.05). While the female/male ratio was 46.2/58.8% in the hypertensive group, it was 79.9/23.1% in the normotensives. The gender ratio of the groups did not show a statistical difference (p>0.05) (Table 1).

Table 1. Demographic characteristics of normotensive and hypertensive patients. Chi-square and Student’s t-test, SD: Standart deviation, Statistical significance: *p<0.05

	Normotensive	Hypertensive	p value
Gender			0.227
Male (n)	10 (79.9 %)	6 (46.2%)	
Female (n)	3 (23.1%)	7 (53.8%)	
Age			*0,000197
Mean±SD	42±8.84	61.69±13.55	

4. DISCUSSION AND CONCLUSION

In this study, it was shown that the discus intervertebralis of normotensive and hypertensive patients who underwent lumbar discectomy were not different in terms of histopathologically and histomorphometrically (in terms of chondrocyte number and lacunae diameter). This is the first study to compare the discus intervertebralis of normotensive and hypertensive patients histopathologically and histomorphometrically.

Although the effects of cardiovascular system diseases such as arterial hypertension and hyperlipidemia on cartilage tissue are known, more studies are needed to detail this relationship. Kabalyk et al. investigated the effects of arterial hypertension on articular cartilage in their experimental study. Researchers have shown in their studies that arterial hypertension damage the articular cartilage histopathologically and histomorphometrically [5]. Our study showed different results from this study. We found that there was no difference between normotensive and hypertensive patients in terms of histopathology, chondrocyte count and lacunae diameter. When we look the reasons for this difference; the first thing that stood out was that while we worked on intervertebral discs, they worked on articular cartilage. There are three different types of cartilage in humans: fibrous, hyaline and elastic cartilage. Articular surfaces are covered with hyaline cartilage. Intervertebral discs are fibrous cartilage. These two cartilages differ histologically. These two cartilage vascularization and nutrition pathways also differ. We think that the difference in results is due to this. The relationship between osteoarthritis and high blood pressure has been the subject of curiosity by many researchers. Ashmeik et al. magnetic resonance imaging in 1126 volunteers showed that increased diastolic blood pressure caused increased articular cartilage matrix damage [9]. Wang et al. and Ashmeik et al. obtained similar results [10]. Ashmeik et al. and Wang et al. obtained very important findings, but these studies are related to articular cartilages like the previous study. The difference between these two studies and our study actually reveals the hypothesis of our future study. In our study, the effects of arterial hypertension on cartilage tissue were similar in men and women. However, Yeater et al. it appears to have obtained different results compared to our study. Yeater et al. showed that hypertension increases osteoarthritis in the articular cartilage in a gender related manner [11]. The presence of serious nervous system problems in discus intervertebralis diseases makes it easier to choose the surgical option in the treatment. Articular cartilage diseases are examined over a longer period of time and after alternative treatments are tried, surgical procedures are applied. The pathophysiological and anatomical differences of these two cartilages lead treatment providers to different diseases and different priorities. These differences perhaps lead the researchers' hypotheses on hypertension and cartilage damage to articular cartilage.

In parallel with our study, Maurer et al. in their magnetic resonance imaging (MRI) study on 400 patients, they

revealed that factors such as obesity, hypertension, diabetes, elevated LDL-c, low HDL-c, elevated triglycerides, smoking status, and alcohol consumption are not related to disc degeneration. Our data support this study histopathologically and histomorphometrically [12]. Although we and Maurer et al. showed that hypertension did not make any difference in intervertebral discs, Samartzis et al. in an MRI scan of 1800 volunteers, they showed that high blood pressure was associated with different stages of lumbar disc degeneration [13]. If different results are obtained with the same methods in science, the existing hypothesis must be repeated. These repetitions will provide us with powerful data in proving or ignoring the hypothesis. Our focus is on a detailed examination of the subject of hypertension and disc degeneration.

The data obtained from this study reveal important results regarding fibrous cartilage histopathology and hypertension. It shows that the fibrous cartilage in the discus intervertebralis of normotensive and hypertensive patients is not different histopathologically and histomorphometrically. Future studies should include larger populations in terms of the number of volunteer patients and advanced imaging techniques such as MRI with molecular examination methods together.

Acknowledgement

The authors thank to Bilecik Seyh Edebali University and Bilecik Training and Research Hospital.

Conflicts of interest

The authors declare that there is no conflict of interest.

REFERENCES

- [1] Grunhagen T, Wilde G, Soukane DM, Shirazi-Adl SA, Urban JP. Nutrient supply and intervertebral disc metabolism. *J Bone Joint Surg Am.* 2006;88(2):30-5.
- [2] Roberts S, Evans H, Trivedi J, Menage J. Histology and pathology of the human intervertebral disc. *J Bone Joint Surg Am.* 2006;88(2):10-4.
- [3] Eygi E, Balkaya AN, Gurbet A, Şahin Ş. Non-Opere Tek Mesafe Lomber Disk Herniasyonlarında Transforaminal Epidural Steroid Enjeksiyonu Etkinliğinin Değerlendirilmesi. *Kocatepe Tıp Dergisi.* 2023;24(2):148-53.
- [4] Khamidov O, Khodzhanov IY, Mamasoliev B, Mansurov DS, Davronov A, Rakhimov A. The role of vascular pathology in the development and progression of deforming osteoarthritis of the joints of the lower extremities (Literature review). *Annals of RSCB.* 2021;25(1):214-25.
- [5] Kabalyk M, Kovalenko T, Nevzorova V, Sukhanova G. Effect of Arterial Hypertension and Hyperlipidemia on the Remodeling of Articular Cartilage and the Development of Osteoarthritis (Experimental Study). *Adv Gerontol* 2020;10(1):79-85.
- [6] Mazurov V, Stolov S, Vorobyeva O, Dolgikh S, Martynov IV, Pobyegai O. Cardiovascular problems

- in rheumatology. *Medical academic journal*. 2009;9(1):59-65.
- [7] Mills KT, Stefanescu A, He J. The global epidemiology of hypertension. *Nat Rev Nephrol*. 2020;16(4):223-37.
- [8] Bilge O, Doral MN, Atesok K, Atay OA, Donmez G, Turhan E, et al. The effects of the synovium on chondrocyte growth: an experimental study. *Knee Surg Sports Traumatol Arthrosc*. 2011;19(7):1214-23.
- [9] Ashmeik W, Joseph GB, Nevitt MC, Lane NE, McCulloch CE, Link TM. Association of blood pressure with knee cartilage composition and structural knee abnormalities: data from the osteoarthritis initiative. *Skeletal Radiol*. 2020;49(9):1359-68.
- [10] Wang Y, Meng T, Ruan G, Zheng S, Zhu J, Cen H, et al. Associations of blood pressure and arterial stiffness with knee cartilage volume in patients with knee osteoarthritis. *Rheumatology (Oxford)*. 2021;60(10):4748-54.
- [11] Yeater TD, Griffith JL, Cruz CJ, Patterson FM, Aldrich JL, Allen KD. Hypertension contributes to exacerbated osteoarthritis pathophysiology in rats in a sex-dependent manner. *Arthritis Research & Therapy*. 2023;25(1):1-13.
- [12] Maurer E, Klinger C, Lorbeer R, Hefferman G, Schlett CL, Peters A, et al. Association between cardiovascular risk factors and degenerative disc disease of the thoracolumbar spine in the general population: results from the KORA MRI Study. *Acta Radiol*. 2022;63(6):750-9.
- [13] Samartzis D, Bow C, Karppinen J, Luk KDK, Cheung BMY, Cheung KMC. Hypertension is Independently Associated with Lumbar Disc Degeneration: A Large-Scale Population-Based Study. *Global Spine Journal*. 2014;4(1).