**Received:** 07 Feb 2023 | **Accepted:** 27 Mar 2023 **Genel Tıp Derg. Volume** 33/**Issue** 3 (June), 299-304
DOI: 10.54005/geneltip.1248667

**ORIGINAL ARTICLE**

# The Assessment of the Effects of Synthetic Collagen Membrane Use on the Prevention of Epidural Fibrosis Development in Patients Undergoing Lumbar Discectomy by Magnetic Resonance Imaging Findings

# Lomber Diskektomi Operasyonu Yapılan Hastalarda Sentetik Kollajen Membran Kullanımının Epidural Fibrozis Gelişimini Önleme Üzerine Etkilerinin MRG Bulguları ile Değerlendirilmesi

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**How to cite ?**

Kaya M. The assessment of the effects of synthetic collagen membrane use on the prevention of epidural fibrosis development in patients undergoing lumbar discectomy by magnetic resonance ımaging findings. Genel Tıp Dergisi. 2023; 33(3)299-304.

**ABSTRACT**

**Bacground/Aims:** The aim of study to evaluate the effects of synthetic collagen membrane placed on dura mater on the prevention of arachnoiditis and fibrosis development by magnetic resonance imaging (MRI) findings in patients undergoing lumbar discectomy.
**Methods:** A total of 40 patients who underwent single level unilateral discectomy for lumbar disc hernia were retrospectively evaluated. Sixteen patients with collagen membranes placed on the dura and 24 patients without any material on the dura were included in the study. Postoperative MRI images of the patients with and without collagen membranes were examined and evaluated whether the material used was effective in preventing arachnoiditis and / or epidural fibrosis and granulation tissue formation.
**Results:** Nine female patients (37.5%) and 15 male patients (62.5%) of 24 patients were in the collagen membrane-free group. Four of the patients in the collagen membrane group were female (25%) and 12 were male (75%). The mean age of the non-membrane group was 35.47 ± 9.06, and the mean age of the membrane group was 37.40 ± 8.92 years. According to MRI findings, granulation tissue and epidural fibrosis were not observed in 8 (50%) of 16 patients with collagen membranes, whereas granulation tissue was observed in 8 (50%) patients. Granulation tissue was not observed in 10 (41.7%) of 24 patients without collagen membrane, whereas epidural fibrosis and granulation tissue formation was observed in 14 (58.3%). Based on these results, there was no statistically significant relationship between type-I collagen membrane use and granulation tissue formation. (P = 0.604 <0.05). There was no difference between the rate of granulation tissue (50%) and absence (50%) in patients with type-I collagen membranes.
**Conclusion:** According to these results and MRI findings, it was found that peroperative type-I collagen membrane use in lumbar discectomy did not have a statistically significant effect on granulation tissue or epidural fibrosis formation.

**Keywords:** lumbar disk herniation, epidural fibrosis, collagen membrane, MRI

**ÖZ**

**Arkaplan/Amaç:** Lomber diskektomi yapılan hastalarda dura mater üzerine yerleştirilen sentetik kollajen membranın araknoidit ve fibrozis gelişimini önlemedeki etkisinin manyetik rezonans görüntüleme (MRG) bulguları ile değerlendirilmesi.
**Yöntemler:** Lomber disk hernisi nedeniyle tek seviyeli unilateral diskektomi uygulanan toplam 40 hasta retrospektif olarak değerlendirildi. Dura üzerine kollajen membran yerleştirilmiş 16 hasta ve dura üzerinde herhangi bir materyal bulunmayan 24 hasta çalışmaya dahil edildi. Kollajen membranı olan ve olmayan hastaların ameliyat sonrası MR görüntüleri incelenerek kullanılan malzemenin araknoidit ve/veya epidural fibrozis ve granülasyon dokusu oluşumunu önlemede etkili olup olmadığı değerlendirildi.
**Bulgular:** 24 hastanın 9'u kadın (%37,5) ve 15'i erkek (%62,5) kollajen membransız gruptaydı. Kollajen membran grubundaki hastaların dördü (%25) kadın, 12'si (%75) erkekti. Membransız grubun yaş ortalaması 35,47 ± 9,06, membranlı grubun yaş ortalaması 37,40 ± 8,92 idi. MRG bulgularına göre kollajen membranlı 16 hastanın 8'inde (%50) granülasyon dokusu ve epidural fibrozis izlenmezken, 8 (%50) hastada granülasyon dokusu görüldü. Kollajen membranı olmayan 24 hastanın 10'unda (%41,7) granülasyon dokusu izlenmezken, 14'ünde (%58,3) epidural fibrozis ve granülasyon dokusu oluşumu gözlendi. Bu sonuçlara göre tip I kollajen membran kullanımı ile granülasyon dokusu oluşumu arasında istatistiksel olarak anlamlı bir ilişki bulunmadı. (P = 0,604 <0,05). Tip-I kollajen membranı olan hastalarda granülasyon dokusu (%50) ve yokluğu (%50) arasında fark yoktu.
**Sonuç:** Bu sonuçlara ve MRG bulgularına göre, lomber diskektomide peroperatif tip-I kollajen membran kullanımının granülasyon dokusu veya epidural fibrozis oluşumu üzerinde istatistiksel olarak anlamlı bir etkisinin olmadığı bulundu.

**Anahtar Kelimeler:** lomber disk hernisi, epidural fibrozis, kollajen membran, MRG

## Introduction

Although low back pain is not a life-threatening problem, it is often observed in developed communities, especially in the working middle-age group, which leads to a loss of labor, as well as a significant financial loss, considering the cost of diagnosis and treatment. It ranks second after upper respiratory tract problems among the reasons for applying to a doctor all over the world. Besides, it ranks third in diseases that require surgical intervention and fifth in diseases that need inpatient treatment. In studies conducted in the

**Peer-Review:** Double anonymized - Two External
**Plagiarism Checks:** Yes - iThenticate
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United States, it was found that 60-90% of individuals in the adult group go to a doctor with a complaint of low back pain for at least once in their lives, and an average of seven million new patients with chronic lombalgia appear every year, and two hundred thousand new lumbar discectomy operations are performed (1-5).

2-3% of lower back pain is due to Lumbar Disc Herniation (LDH), and an average of 15% of lumbar disc herniation undergo surgery. Due to the formation of peridural granulation tissue as a result of fibrosis in the surgical area after lumbar discectomy, patients may continue to complain of dysesthesia reflected in the waist and lower extremities. A complaint of ongoing pain after lumbar surgery leads to a deterioration in the quality of life of patients, causing them to take medication for a long time and sometimes have re-surgery (6).

The peridural lesion fibrosis, which occurs in the surgical field after surgical intervention and is responsible for pain pathogenesis, is known as adhesive arachnoiditis. The rate of peridural fibrosis and adhesive arachnoiditis is reported with a rate of 25%. The inflammation of the arachnoid membrane is called arachnoiditis, and the development of scar tissue extradural on the thecal sac or around the nerve root is called peridural fibrosis. In the USA, 250 thousand individuals annually undergo a laminotomy or laminectomy surgery for LDH alone (1). When laminectomies performed for scoliosis, lumbar spinal stenosis, spinal traumas, and spinal tumors and similar reasons are added to LDH, a significant number of patients are exposed to the risk of peridural fibrosis and arachnoiditis (4).

MRI is the most popular method for advanced imaging of lumbar disc hernias. MRI offers three-dimensional and detailed information about the anatomy of the lumbar spinal region. MRI allows the physicians to see soft tissues and degenerative changes of the disc in more detail than computed tomography. It can distinguish free fragments (sequestration) from extruded disc hernias. Neural involvement can be detected in the spinal canal, foraminal, or extraforaminal. Magnetic Resonance Imaging is very useful in distinguishing disc herniation from tumors, vascular abnormalities, or bone compression (7).

Under current conditions, there is no effective medical or surgical treatment for epidural fibrosis. The goal of treatment is to minimize epidural fibrosis. The main goals are prevention of fibrosis, epidural lysis, medical and surgical treatment. The most important factor in minimizing epidural fibrosis is to use of a non-traumatic surgical technique. The main sources of epidural fibrosis are fibrogenic stimuli such as a residual disc fragment, damaged paravertebral muscle-derived fibroblasts, and hematoma-derived fibrin (8,9). The aim of preventive treatment should be to eliminate the fibrogenic stimulus (10). Thus, the amount of anterior epidural fibrosis can be minimized.

Many studies have investigated the effectiveness of various treatments to prevent epidural fibrosis. A wide variety of materials have been used to prevent or reduce scarring as mechanical barriers that limit the attachment of neural elements. Among these are biological (fat graft), soft non-biological (absorbable gelatin spongel, bone wax), solid non-biological (polymethylmethacrylate, membranes, polytetrafluoroethylene), and viscous materials (collagen-based material, hyaluronic acid, carboxymethylcellulose, carbohydrate polymer, ADCON-L) (11). The results of these studies have shown only moderate success in inhibiting epidural fibrosis.

The arachnoid mater is a thin, fibro cellular layer that is in direct contact with the dura mater. In arachnoiditis, the severity of the disease can range from focal adhesions to intensive scars. The main treatment of arachnoiditis is the conservative approach. However, some authors have reported a temporary decrease in symptoms with oral steroid therapy (12). Besides, satisfactory results of intrathecal hyaluronidase have been reported, but this has not been widely adopted (13). The reliability of intrathecal steroid administration is limited due to reports of arachnoiditis following spinal steroid administration. Another approach is to treat lumbar arachnoiditis with arachnoid lysis as a surgical option.

The terms epidural fibrosis and arachnoiditis are generally interrelated and used interchangeably. Arachnoiditis is a chronic process that develops in the dura and is the inflammation of the arachnoid membrane. It can grow without surgical intervention. Epidural fibrosis, on the other hand, is extradural and usually grows out of the surgical process. The terms adhesion or scar tissue are also used instead of epidural fibrosis. In cases where epidural fibrosis and arachnoiditis are experienced together, the patient is usually diagnosed with epidural fibrosis, and arachnoiditis is ignored. However, considering the long-term results, arachnoiditis is a more severe inflammation than epidural fibrosis in terms of complications. Although the symptoms of epidural fibrosis are similar to arachnoiditis, they are usually local. The symptoms associated with arachnoiditis, on the other hand, can spread along the nerve path in a more diverse perspective and over a wider area. The aim of this study to examine retrospectively the presence of arachnoiditis, peridural fibrosis, and/or granulation tissue in postoperative MRI images with a group of patients who underwent a single-level lumbar discectomy operation and placed a Type I Collagen membrane on a peroperative dura.

In this study evaluated retrospectively the presence of arachnoiditis, peridural fibrosis, and/or granulation tissue in postoperative MR images of the patient group who underwent a single-level lumbar discectomy operation and Type I Collagen membrane was placed on the peroperative dura, and the patient group who were not placed collagen membrane on the dura, and we aimed to investigate the collagen membrane's ability to prevent this pathological process.

## Methods

### Study Selection

Sixteen patients who underwent single-level lumbar discectomy between January 2016 and October 2018 at the Department of Brain and Nerve Surgery, Faculty of Medicine, Selçuk University, and implanted a collagen membrane on the dura and 24 patients who were not implanted collagen membrane were included in this study.

Criteria for inclusion in the study: The study included 40 patients aged over 18 and under 65 who had a single-level, unilateral microscopic discectomy operation due to lumbar disc herniation and had no previous history of spinal surgery.

Criteria for exclusion in the study: Patients with a previous history of spinal surgery, multi-level lumbar disc herniation, patients over 65 and under 18 years of age, and patients with previous findings of preoperative arachnoiditis or epidural fibrosis were not included in both groups of the study. In addition, patients who developed a dural tail during surgery and associated cerebrospinal fluid were not included in the study.

### Research Plan

40 patients who underwent single-level, unilateral lumbar discectomy for lumbar disc herniation were retrospectively analyzed in our clinic. A group of 16 patients with collagen membrane placed on the dura peroperatively and 24 patients in whom no material was placed on the dura were included in the study. Postoperative MR images of patients with and without collagen membrane were analyzed together with the Radiology Department of Selçuk University Medical Faculty Hospital, and it was investigated whether the material used was effective in preventing arachnoiditis and/or epidural fibrosis and granulation tissue formation.

### Research Methodology

Surgical and postoperative approach: All patients included in the study were placed on the operating table in the prone position under general anesthesia. The lumbar region was painted with sterile solutions and covered with sterile greens. After determining the distance with the help of fluoroscopy, an approximately 5 cm long incision was made in the lumbar region vertically in the midline, corresponding to the herniated disc vertebrae. After the skin and subcutaneous passage, the paravertebral muscles were removed with the help of a periosteum spoon and gauze. After cutting the paravertebral muscle fascia using Madson scissors, it was scraped towards the side of the herniated disc. After determining the corresponding facet joint and pedicle using fluoroscopy again, a Taylor retractor was placed. Then the operation was continued with the help of a microscope. Following the partial hemilaminectomy, flavectomy was performed using a microscope, and the dura mater was seen. 1/3 medial facetectomy and undercutting was performed. By performing foraminotomy, the subligamentous extruded disc fragment in the epidural area was removed with the help of a hook and a dissector. Discectomy was performed in the relevant vertebral area after the distance was determined again by fluoroscopy. When the dura and root were seen to be relieved, bleeding was controlled. One synthetic Type I collagen membrane was cut and placed in the epidural area in the patient group in which the material was used. Then the Taylor retractor was removed from the surgical field, and the layers were sutured in the anatomical plan in accordance with the procedure by performing hemostatic control again. The patient was turned to the supine position. Following the reanimation, the patient was extubated, and no additional neurodephicitis was observed postoperatively. Erythrocyte suspension was not used in both groups included, and they were followed-up in the service.

Mobilization was restricted to all patients in the early postoperative period. Tramadol hydrochloride, paracetamol, and 1st generation cephalosporin were preferred as analgesics. Patients were mobilized 3 times a day on the 1st postoperative day and discharged on the 2nd postoperative day. The dressing was performed daily for the first 15 days after the operation, and patients were advised to keep the operation site dry. They were also told not to lift heavy for the first 45 days except for daily necessities.

Magnetic Resonance Imaging (MRI): In the study, all 40 patients who underwent a single-level discectomy due to LDH underwent MRI between the postoperative 8th and 10th weeks. MRI results were evaluated in detail together with the radiology department and evaluated whether the use of collagen prevented the development of epidural fibrosis (Figure 1).

Collagen membrane: The collagen membrane used in the study was cut and placed in the peridural area to cover the exposed dura (Figure 2. and Figure 3.). Care was taken to place the membrane so that it could adhere to the dura and contact with blood. Bleeding control was performed for paravertebral muscles to prevent blood leakage into the field. In addition, hemostasis was achieved by applying bone wax to the bone areas where laminectomy was performed.

### Statistical Analysis

A chi-square test was performed to examine the relationship between the use of Type I collagen membranes and the formation of granulation tissue. Statistical results were presented in the tables in frequency (n) and percentage (% ), and the value $p<0.05$ was taken into account for statistical significance. A bar chart was drawn for the visual presentation of the information obtained as a result of the research analysis. The R Version 3.5.1 software was used in statistical analysis.

## Findings

A total of 40 patients, 13 female (32.5%) and 27 male (67.5%), who underwent unilateral discectomy for lumbar disc herniation, were included in the study.

Of the 24 patients in the group without collagen membrane, 9 were female (37.5%) and 15 were male (62.5%). In the group in which the collagen membrane was used, 4 of the patients (25%) were female (25%) and 12 were male (75%). The age range of the group without membrane was 22-52 years, with a mean of 35,47±9,06. The age range of the group with the membrane was 25-51 years, with a mean of 37,40±8,92. There was no statistically significant difference in the age range of both groups (Table 1. and Table 2.)

A chi-square test was used to examine the relationship between the use of Type I collagen membrane and the formation of granulation tissue. According to statistical analysis, granulation tissue and epidural fibrosis were not observed in 8 (50%) of 16 patients in whom the collagen membrane was used in single-level, unilateral lumbar discectomy, while granulation tissue was observed in 8 (50%) of them. While granulation tissue was not observed in 10 (41.7%) of 24 patients in whom a peroperative collagen membrane was not used, epidural fibrosis and granulation tissue formation were observed in 14 (58.3%) (Table 3.).

**Discussion**

Low back pain is one of the most common complaints in society that restricts business life. Although its prevalence peaks in adults between the ages of 45 and 64, up to 84% of adults in the United States describe a complaint of low back pain at least once in their lifetime (14,15). Epidural fibrosis and granulation tissue formation is a common condition after lumbar disc herniation. Long-term results after surgical treatment of disc herniation showed that approximately 10% of patients did not completely achieve positive results. One explanation for these results is epidural fibrosis, which occurs during the recovery period after surgery (16). Epidural fibrosis fails in about 14-15% of cases (17,18). In addition, it disrupts the natural plan of the dissection due to reasons such as scar and adhesion between tissues and makes revision surgeries significantly difficult (19).

In an experimental study conducted in 1997, Einhaus et al. found that ADCON-L is effective in preventing epidural fibrosis and scar formation (84). In another prospective, double-blind, controlled study conducted in 1998, Porchet et al. noted that epidural fibrosis after surgery was less in patients undergoing ADCON-L after spinal surgery than in the control group (20).

Although ADCON-L can reduce fibrosis by filling gaps in the laminectomy area, it has been shown that it can prevent long-term dural tears healing in this area and cause a foreign body reaction (21, 22). It was also stated that it could cause a cerebrospinal fluid leak, and its use is not common for reasons such as high cost and difficulty supplying it (23).

In their experimental study in 1990, Songer et al. evaluated sodium hyaluronic, a 1.9% solution for delaying peridural fibrosis after unilateral lumbar hemilaminectomy, annular fenestration, and nuclectomy in dogs. The 3 materials of fat grafts, gel foam, and sodium hyaluronate were compared with controls without any material for their ability to inhibit peridural fibrosis, and they found that sodium hyaluronate inhibits peridural fibrosis more than other materials at both macroscopic and microscopic levels. They also indicated the area of peridural fibrosis in the sodium hyaluronic group and the degree of adhesion in dissection in significantly fewer levels (24).

One of the materials studied in the prevention of peridural adhesion is the Gore-Tex membrane in polytetrafluoroethylene (ePTFE) structure. This membrane is also used to prevent adhesions in abdominal surgery and cardiovascular surgery. Sixty-six patients in whom the Gore-Tex membrane was laid over the decompressive laminectomy or hemilaminectomy defect and sutured to the facet capsule were evaluated in a clinical study, and it was observed that both peridural fibrosis and radicular pain in the treatment group were lower than the control group (25). Nevertheless, in some other studies, it was observed that the ePTFE membrane was not sufficiently effective in preventing peridural fibrosis (26).

A gel combination consisting of the Oxiplex adhesion barrier of Carboxymethyl Cellulose (CMC) and Polyethylene Oxide (PEO) was evaluated for the reduction of peridural fibrosis and leg pain after surgery. In some experimental studies, it was also noted that the number of areas without epidural fibrosis and the severity of fibrosis (adhesions) decreased among the activity parameters of gel and film combinations (27).

An experimental study was designed by Nussbaum et al. (1990) to compare the effectiveness of VICRYL (polyglactin 910) mesh and autogenous fat graft in minimizing postoperative epidural scarring. It was stated that VICRYL mesh might be a safer method to limit epidural scar formation compared to the use of free fat grafts after laminectomy in dogs (28). In another similar experimental study, Akdemir et al. (1993) reported that VICRYL mesh applied to laminectomy areas could be an alternative method to minimize postoperative epidural scar formation (29). However, reviews on this subject were limited to experimental studies.

Impaired fibrinolytic activity after lumbar disc surgery was shown to be correlated with scarring. In previous studies, impaired fibrinolytic activity was significantly correlated with chronic low back pain syndromes and poor results of lumbar disc surgery. It was suggested that a fibrinolytic defect would cause insufficient removal of fibrin deposits, as well as lead to a long-term inflammatory reaction, the formation of large scar tissue, and the operation to give a failed result (30). For this purpose, recombinant tissue plasminogen activator (rt-PA) was used in various experimental studies to prevent epidural fibrosis and scarring. In an experimental study performed on 40 rats, Çekinmez et al. (2008) showed that there was inhibition in the formation of epidural fibrosis in the control and rt-PA groups 6 weeks after the operation.

The effectiveness of mitomycin-C, a chemotherapeutic agent, in terms of preventing peridural fibrosis after laminectomy was investigated in various studies. For this purpose, in their study in 2003, Doğulu et al. applied cotton pads soaked with 0.02% mitomycin C and saline to the operation field on 12 rabbits that underwent L4 laminectomy. One month after the operation, the extent of peridural fibrosis was evaluated and analyzed histologically. In histological examinations, it was observed that peridural fibrosis was significantly reduced in areas treated with mitomycin-C (31).

In another similar study, Sun et al. (2007) compared the effectiveness of mitomycin-C or 5-fluorouracillin (5-FU) topical administration in preventing peridural fibrosis after laminectomy. It was observed that there was no significant adhesion in rats in the group of mitomycin-C, but severe peridural adhesions were found in the 5-FU and control groups (32).

Boric acid is considered an effective agent due to its anti-inflammatory and antioxidant properties and was used to prevent epidural fibrosis. In a new study conducted with rats in 2019, 2.5% boric acid solution and 5% boric acid solution were added to the L3 level after laminectomy, and epidural fibrosis level was evaluated macroscopically and histopathologically after 4 weeks. Consequently, boric acid reduced epidural fibrosis in rats after laminectomy. In addition, the effect of a 5% boric acid solution was more apparent compared to a 2.5% solution (33). Although these products have been proven effective through randomized clinical trials, they are likely to be part of routine management of epidural fibrosis, but there is little data available on long-term results and complications of these procedures.

In this study, we retrospectively examined 40 patients operated due to LDH. 16 patients were placed with Type I collagen membranes to prevent epidural fibrosis or scarring, while 24 patients did not have any material placed in the peridural area. Postoperative MRI taken between the 6th and 8th weeks was evaluated as epidural fibrosis and/or scar formation or no epidural fibrosis and/or scar formation together with the radiology department, and the results were statistically calculated.

According to statistical analysis, 8 (50%) of 16 patients in whom we used Type I collagen membranes in a single-level, unilateral lumbar discectomy did not experience granulation tissue and epidural fibrosis according to MRI findings, while granulation tissue was observed in the other 8 (50%). Of the 24 patients in whom we did not use peroperative collagen membranes, 10 (41.7%) did not have granulation tissue, while 14 (58.3%) had epidural fibrosis and granulation tissue formation. Based on these results, no statistically significant correlation was found between the use of Type I collagen membranes and the formation of epidural fibrosis and/or scarring.

**Conclusion**

In this study 16 patients in whom Type I collagen membrane was used on the dura during lumbar discectomy and 24 patients in whom no material was placed in the epidural area were examined retrospectively. According to MRI findings, it was found that the use of the Type I collagen membrane did not have a statistically significant effect on preventing the granulation tissue or epidural fibrosis formation. More clinical or experimental studies on the collagen membrane are needed in the coming years, and its place in clinical use should be determined by further assessments.

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