Association Between Peridural Scar and Recurrent Radicular Pain After Lumbar Discectomy: Magnetic Resonance Evaluation

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Abstract

THE PURPOSE OF this study was to investigate the presence of any correlation between recurrent radicular pain during the first six months following first surgery for herniated lumbar intervertebral disc and the amount of lumbar peridural fibrosis as defined by MR imaging. 197 patients who underwent first-time single-level unilateral discectomy for lumbar disc herniation were evaluated in a randomized, double-blind, controlled multicenter clinical trial. Clinical assessments, performed by physicians blinded to patient treatment status, were conducted preoperatively and at one and six months postoperatively. The enhanced MR images of the operative site utilized in the analysis were obtained at six months postoperatively. Radicular pain was recorded by the patient using a validated visual analog pain scale in which 0 = no pain and 10 = excruciating pain. The data obtained at the 6 month time point were analyzed for an association between amount of peridural scar as measured by MR imaging and clinical failure as defined by the recurrence of radicular pain. The results showed that the probability of recurrent pain increases when scar score increases. Patients having extensive peridural scar were 3.2 times more likely to experience recurrent radicular pain than those patients with less extensive peridural scarring. In conclusion, this prospective, controlled, randomized, blinded, multicenter study has demonstrated that there is a significant association between the presence of extensive peridural scar and the occurrence of recurrent radicular pain.

Postoperative fibrosis is a consequence of surgical procedures and can cause clinically important sequelae due to formation of adhesions between tissues or due to compression of organs and other anatomic structures by dense fibrotic scar. In the case of lumbar spine surgery, there are numerous
reports suggesting that fibrosis and adhesions can cause compression or tethering of the nerve root, which may cause recurrent radicular pain and physical impairment. The literature does not establish a definite rate of fibrosis-related problems following lumbar discectomy, but it is repeatedly suggested that fibrosis may be a major cause of recurrent symptoms when no alternative bony or disc pathology can be discerned \((2, 3, 7, 9, 14, 19, 20, 22, 25, 28, 29, 38)\). While it has been suggested that fibrosis may be causal in as much as 24% of all failed back surgery syndrome cases \((6, 35)\), no previous studies have provided proof of a correlation between peridural scar and recurrent radicular pain. It is important to note, however, that previous studies to evaluate peridural fibrosis related problems have been hampered by small sample size, retrospective designs, or the lack of quantitative imaging of the amount of peridural scarring. This present study does not have these limitations since it was a prospective, randomized, double-blind clinical trial with a large sample size and used contrast-enhanced MR imaging to quantitate peridural scar. The purpose of the analysis reported here was to evaluate the presence of any association between recurrent radicular pain during the first six months following surgery for herniated lumbar intervertebral disc and the amount of lumbar peridural scar as defined by MR imaging.

**PATIENTS AND METHODS**

**Clinical Study Design**

The study population was from a prospective, randomized, double-blind, controlled multicenter clinical trial evaluating the safety and effectiveness of an anti-adhesion barrier gel, ADCON-L, in preventing peridural fibrosis and dural adhesions following single-level unilateral discectomy for first-time lumbar disc herniations. Nine neurosurgery centers in three countries (Table 1) participated in this study.

The study design was reviewed by each investigator and each center's Ethics Committee in accordance with good clinical practices. Informed consent was obtained from each patient and the study data monitored for accuracy. Clinical assessments, performed by physicians blinded to patient treatment status, were conducted preoperatively and at one and six months postoperatively. MRIs of the lumbar spine were obtained, without and with gadolinium enhancement \((0.1 \text{ mmol/kg})\), preoperatively and at six months postoperatively. The MRIs were evaluated by a neuroradiologist blinded to patient treatment status. The six month evaluation time was selected for the effectiveness analysis because the literature indicates that postoperative fibrosis stabilizes by 6 months, with no further changes at 12 months. Unpublished data from this study confirms this time course. ADCON-L is a gel which is completely resorbed within 1-2 months following surgery. Thus the MR examination at 6 months post surgery was not biased by the presence of this material.

Patients were included in the study if they met all the following inclusion criteria: first lumbar surgery, symptoms of radiculopathy, radiological signs consistent with clinical pattern, single level, unilateral herniated disc, patient age of 18 to 60 years, and failure of at least 2 weeks of nonsurgical care or the urgent need for surgery. Patients were excluded from the study if they had any of the following: multilevel, far lateral, or bilateral disc herniation, significant spinal degenerative disease or scoliosis, prior percutaneous nucleotomy or chemonucleolysis, treatment
with peridural steroid within the prior month, recent oral steroids or NSAID's within the prior 24 hours or the occurrence of a dural nick during surgery. The exclusion criteria were focussed on assuring 1) a pristine patient population without prior spine surgery, and with well-defined radicular symptoms, and 2) the minimization of any potential problems related to wound healing. A total of 197 patients were included in the analysis reported herein.

Methodology

All surgeries were performed via midline approach. Surgeons were free to perform whatever degree of laminectomy was necessary to assure adequate visualization and ultimate decompression of the affected nerve root, and all findings and procedures were recorded on case report forms. Following randomization assignment, patients either received the treatment (ADCON-L) or had nothing instilled into the surgical site. The surgical site was then closed in a routine fashion. The surgeon was unaware which treatment arm each patient was in until completion of the surgical decompression and just prior to closure. The 6-month clinical evaluation was conducted by a qualified individual other than the surgeon who performed the surgery. The patients and evaluators remain blinded to the treatment arms. Patients were not remunerated for participation in the study.

Radicular pain was reported by the patient using a validated visual analog pain scale (VAPS) in which 0 = no pain and 10 = excruciating pain (32). The patient drew a line through the scale at the position that most accurately described the level of pain he was trying to relate. Patients were asked to report three slightly different aspects of their radicular pain using this scale: "pain when most severe"; "pain on average" and "pain at the end of the day". Only the first two measures were studied.

Recurrent radicular pain was defined as follows: 1) the patient had a successful outcome from primary surgery as determined by a radicular pain score (VAPS) of <= 4 at the 1 month postoperative evaluation; 2) the patient had a recurrence of radicular pain as defined by a VAPS score of > 4 at the 6 month postoperative evaluation; patients with evidence of residual or recurrent intervertebral disc herniation as determined by MR imaging were excluded from analysis.

MR Evaluation

All MR studies were performed on commercial superconducting units using an 8 inch elliptical spine surface coil or equivalent. MR examinations followed a standard protocol at each clinical site (Table 2). Axial images were obtained in a gap and fill fashion, to allow complete coverage of the operative site and were contiguous (i.e., not only disk space levels). Axial images covered at least one level above the operative site to one level below the site (except for L5-S1 where the caudal most slice was to the mid S1 body).

Evaluation of all MR images was performed by one reader (JSR), blinded to treatment arm and to clinical findings. The MR scar evaluation details the location of peridural fibrosis into 5 contiguous axial slices centered about the intervertebral disk, and further subdivides each slice into 4 quadrants defined by perpendicular lines drawn from the central aspect of the thecal sac (Fig. 1). If the thecal sac was obscured by postoperative changes, then the quadrant lines were drawn from the expected central point of the thecal sac. The posterior margin of the peridural evaluation site (at the laminectomy level) was defined by a line drawn between the most posterior aspects of the remaining bony lamina. The amount of peridural scar was graded on a scale of 0 to
4 for each quadrant (see Fig. 2 for examples) at each imaging slice encompassing the operative level:

0 = no/trace scar
1 = >0% and <= 25% of quadrant filled with scar
2 = >25% and <= 50% of quadrant filled with scar
3 = >50% and <= 75% of quadrant filled with scar
4 = >75% of quadrant filled with scar

The criteria for identifying peridural scar were as follows: peridural scar is iso- to hypointense relative to intervertebral discs on T1-weighted MR images. Peridural scar tends to form a curvilinear pattern surrounding the dural tube and is fairly homogeneous. The presence or absence of mass effect is not a diagnostic criterion, since both scar and herniated discs may show mass effect. Retraction of the dural tube toward the side of the soft tissue is a criterion for scar. Scar tissue is seen to consistently enhance immediately after the injection of contrast material, regardless of whether the scar is anterior, lateral or posterior to the thecal sac. Recurrent herniated disc material is isointense to the intervertebral disc proper on T1-weighted images and may have a variable appearance on T2-weighted images varying from low signal intensity to high signal intensity. Recurrent herniations tend to have a polypoid configuration, with a smooth outer margin. Recurrent residual disc material does not enhance within the first ten to twenty minutes following the administration of contrast material (13, 30).

Assumptions

An assumption of the study group was that any clinical effect of peridural scar would be manifested not on the initial (1 month) postoperative evaluation (since scar would not have had a chance to form), but rather at the 6 month evaluation when peridural scar is mature. Patients whose pain rating did not improve following surgery were excluded, as were patients with MRI evidence of residual or recurrent herniations at 6 months postoperatively. The small number of patients falling in the above 2 excluded categories were assumed to represent surgical failures. Therefore, patients analyzed in this study were those who showed improved pain scores (<=4) on the visual analogue scale at one month postoperatively.

Statistical Methods

The relationship between the amount of scarring at six months and radicular pain at six months was evaluated by computing the Spearman correlation coefficient for each clinical center, then combining the results across centers using the method of Han (12). The hypothesis that the combined correlation coefficient equals zero was then tested. To assess the predictive value of the amount of scarring on recurrent radicular pain, logistic regression analysis was used. The significance of the coefficient for scarring was assessed with a likelihood ratio test. The Hosmer-Lemeshow goodness-of-fit statistic was used to check the fit of the model. Finally, to assess the relationship between the presence of extensive scar and recurrent radicular pain, a Pearson chi square test was used. Due to the relatively small number of patients experiencing recurrent radicular pain, analysis involving this outcome variable could not be adjusted for clinical center. The pain on average and pain when most severe measures were both analyzed, but only the pain when most severe measure showed significant correlation with amount of scar. The data presented in the results section refers to the pain when most severe measure.

RESULTS
The demographics of the patients in the clinical trial are summarized in Table 3. The final database analysed included 197 patients for whom both radicular pain data and MRI's were available. The mean age was 39 years; 60% of the patients were males. The average preoperative radicular (“most severe”) pain score was 7.7.

Type of surgery was not a significant variable in the explanation of recurrent radicular pain. However, the amount of scarring was a significant predictor of recurrent radicular pain. Table 4A summarizes the data for recurrent radicular pain versus scar score. From the fitted logistic regression model, the odds ratio for scar was 2.02 (95% confidence interval of 1.05-3.92), suggesting that for every 25% increase in scarring, the risk of recurrent radicular pain increases 2.02 times (p = 0.036).

Patients with extensive scar score (scar score of 4, denoting more than 75% of the MR quadrant filled with scar) were 3.2 times more likely to experience recurrent radicular pain (“most severe”) than those patients with a scar score of less than 4 (16.7% vs. 5.3%, respectively, p = 0.009)(Table 4B).

Restriction of these analyses to those patients randomized to the control arm of the study revealed the same trends between recurrent radicular pain and scarring. Logistic regression suggested the same increase in risk for recurrent radicular pain with increase in scar as for the total group of patients but this did not reach significance (odds ratio = 2.01, p = 0.134). Control patients with extensive scar were 3.7 times more likely than those with less scar to experience recurrent radicular pain (22% vs. 6%, p = 0.034).

**DISCUSSION**

Lumbar peridural scar occurs after lumbar discectomies and is a replacement of the normal epidural fat with postoperative fibrotic tissue. This peridural scar is capable of binding the dura and nerve roots to the circumferentially surrounding structures and is believed to be one of the major causes of recurrent radicular pain after lumbar laminectomy and discectomy. The scientific literature provides substantial, albeit circumstantial, support to the concept that excessive scar tissue may lead to untoward symptomatology. Nerve fibers encased in collagenous scar tissue suffer an increase in neural tension, impairment of axoplasmic transport and restriction of arterial supply and venous return. Spinal nerve roots and dorsal root ganglia are particularly sensitive to mechanical deformation due to intraspinal disorders (27). Even very low pressures may impair the overall nutritional transport to the nerve roots. Compression of nerve tissue, furthermore, can induce clinical symptoms such as numbness, pain and muscle weakness (27,36).

There is considerable suggestion in the literature (7, 14, 20, 22, 25, 33, 38) that peridural scar formation after disc surgery contributes significantly to unfavorable outcome and recurring symptoms. North et al(1991), for example, reported that favorable outcome for the patients they evaluated was associated with absence of peridural scar requiring surgical lysis. Hurme et al (1991) examined 40 patients five years after their primary surgery for herniated lumbar disc. Eighteen of these patients were graded as having poor results, and an increased amount of scar tissue was found to correlate with poor result.

Indeed, much effort has been devoted to finding materials or procedures that might decrease the amount of peridural scar or keep scar from forming dense adhesions to the dura (11, 15-18, 21, 26, 39). A variety of materials, including silastic, dacron, methacrylate, bone graft, synthetic membranes and foams, free and pedicle fat grafts, carboxymethylcellulose, elastase, and sodium hyaluronate have been evaluated in an effort to stop or limit peridural scar.
Many spine surgeons believe that peridural fibrosis contributes to recurrent radicular pain, particularly when such pain recurs without evidence of reherniation, but this connection has remained speculative and controversial without data showing a statistically significant association. No large controlled study specifically attempting to quantify peridural scar and determine its correlation with clinical sequelae has been conducted before. The enhanced MR imaging technology required to conduct such a study has only recently become available.

For spinal disorders conventional radiographs and myelography have been almost completely replaced by CT and magnetic resonance imaging (MR). MR is now the procedure of choice for lumbar spine imaging (5, 13, 24, 30). CT with intravenous contrast has an accuracy of 67% to 100% in distinguishing scar from disc (4, 37). This technique, however, is technically demanding and involves a large contrast load and single plane imaging. MR without intravenous contrast is at least equivalent to contrasted CT in distinguishing scar from disc (13, 34). The use of gadolinium enhanced MR in the evaluation of scar versus disc has been examined by a number of investigators (1, 4, 5, 13, 24, 30), and the combined results give pre- and post-contrast MR 96% accuracy in differentiating scar from disc.

In the present study, pre- and post-contrast MR imaging was used to provide a measure for the amount of scar at the operative site for each patient and scores for radicular pain were obtained for each patient. Criteria for the determination of the incidence of recurrent radicular pain were also established. When the radicular pain scores were analyzed versus the scar scores for each patient, a significant linear correlation was not apparent. This is not surprising since scar does not always induce pain and other factors may also contribute to pain. On the other hand, the results clearly demonstrated that increasing scar scores led to a significantly increased likelihood of experiencing recurrent radicular pain.

While we believe that this work overcomes many of the shortcomings in previous studies, there are, of course, still some limitations to the present study. No attempt was made to quantitate the amount of peridural fibrosis through area or volume measurements. Such an undertaking would be complicated by the normal variability of the peridural space size, as well as limitations in precisely defining the edges of the fibrosis. This is a potential area for future study.

In summary, the present study is the first study to quantify peridural scar and evaluate its correlation with clinical sequelae, specifically postoperative recurrent radicular pain. This study utilized gadolinium-enhanced MR imaging to quantify peridural fibrosis and has provided definitive evidence for what surgeons have so long suspected. We have demonstrated in a large, prospective, controlled, randomized, blinded, multicenter study that there is a significant association between extensive peridural scar and the occurrence of recurrent radicular pain.

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REFERENCES


Scar is an inevitable accompaniment of lumbar disc surgery but the vast majority of patients are relieved of their pain after discectomy in spite of the presence of scar. When pain recurs or persists after discectomy, magnetic resonance imaging (MRI) with comparison of unenhanced and gadolinium enhanced studies is the diagnostic modality of choice to determine the etiology of the patient's symptoms. As the authors of this paper note, the contribution of peridural fibrosis around the lumbar nerve roots to postoperative pain is controversial. Although scar does not always induce pain, the authors' data showing a linear correlation between the quantity of scar and the severity of pain is quite convincing. This study further confirms the etiology of scar as a cause of pain after discectomy. The reader should remember, however, that despite the presence of enhancement in an epidural mass, a recurrent or residual disc herniation may still be present. We have reoperated on several patients with large masses producing nerve root displacement and have found recurrent disc herniations in spite of the enhancement of the lesions with intravenous gadolinium. Whether reoperation should be considered in patients with extensive epidural scar remains controversial at this time. It will be interesting to see whether ADCON-L is safe and effective in reducing the incidence of symptomatic epidural scar.

Paul R. Cooper
New York, New York

This intriguing study correlates excessive postoperative scarring with recurrent radicular symptoms following discectomy. The data suggest a causal relation between excessive postoperative scar and recurrent radicular pain. This cause-effect relationship, however, is far from clear as their data point out. Only a small fraction of patients with extensive scar (19.4%), for example, reported recurrence of radicular pain. Further, as the authors note, the relationship between scar and recurrent radicular pain was not linear but possibly reflected a “threshold” effect. Nevertheless, 6% of patients with less extensive postoperative scar also experienced recurrent radicular symptoms.

This study also raises clinically relevant issues related not only to the factors which influence postoperative scar formation but their possible modification. These may include patient humoral or immunologic factors, size and duration of the disc herniation, amount and technique of soft tissue and disc dissection, perioperative steroid treatment, and postoperative mobilization and activity levels. It is this reviewer's notion that the degree of postoperative scarring is, at least to some degree, related to intraoperative trauma. I wonder whether extensive disc space dissection and aggressive endplate curettage, while perhaps reducing the risk of recurrent disc herniation, may result in a more exuberant perioperative inflammatory response and increased scar formation. The extensive post-operative epidural scarring associated with posterior lumbar interbody fusion may support this view and, at least partly, explain the relatively frequent occurrence of postoperative radiculopathy experienced in some of these patients.

Paul C. McCormick
New York, New York

Many have felt that fibrosis and adhesions following lumbar disk surgery can cause compression or tethering of nerve roots which may cause significant radicular symptomatology. This
A prospective, controlled, randomized, blinded, multicenter study reviewed this in 197 patients undergoing disc surgery. In this review, the amount of postoperative scar was quantified with postoperative MRI evaluation. Patients with extensive scar were 3.2 times more likely to experience recurrent radicular pain than those patients with significantly less epidural changes. To my knowledge, this is the first study that has attempted to quantify the epidural scar tissue and correlate it with the amount of postoperative radicular symptoms.

In addition to relating some of the postoperative symptoms to the development of peridural scarring, this review brings out several other valuable points. Specifically, there were 20 patients of the 197 studied that had recurrent radicular pain. Even in the group with relatively little epidural scar, there were 6 patients of 113 (5.3%) that had recurrent radicular pain. In summary, 10% of this patient population had significant recurrent radicular pain. Yet when we look at a group of patients undergoing posterior cervical root decompression, the likelihood of recurrent radicular pain is extremely small (probably about one-tenth that described for recurrent lumbar pain in this study), and I suspect that there is a rather similar degree of epidural scarring in the cervical and lumbar region. It is curious why there should be such a difference in outcome of cervical and lumbar root decompression when one would expect the likelihood of postoperative peridural fibrosis to be rather similar. This study supports what many have suspected for some time, and yet it also points out that all failures do not seem related to apparent peridural fibrosis. Certainly anything that can be done to decrease the amount of peridural fibrosis would seem a reasonable goal. Although most of us might expect that the peridural fibrosis actually is the cause of the pain in some of these patients, it is possible that this peridural fibrosis, at least in some patients, is just a marker for more extensive epidural dissection at the time of disc surgery. It may be that this more extensive dissection at the time of surgery is the cause of some residual or recurrent nerve root symptoms rather than the scar itself.

Nevertheless, postoperative epidural changes and possible modifications or differences in surgical technique can affect the amount of epidural changes and the number of patients with significant recurrent radicular pain.

Michael J. Ebersold
Rochester, Minnesota

In this elegant prospective study, the authors conclude that 6 months postoperatively 1 in 10 patients will have recurrent pain after an initial lumbar discectomy and that then there is a 75% chance that extensive scar tissue will be found on the MRI. However, one could also look at these findings from the other side of the coin; that is, 84 of 197 patients had extensive scar tissue on postoperative MRI at 6 months and 83.7% of the time it is asymptomatic. Consequently, even though the authors state that there was a significant association between extensive peridural scar and the recurrence of radicular pain, if a patient has extensive scar tissue on MRI, 83.7% of the time he or she will be asymptomatic. One therefore has to rely on the clinical examination to determine if the patient falls into the 16.3% group with extensive scar tissue and recurrent radicular pain. The difference between the asymptomatic and the symptomatic patient who both have extensive scar tissue? Obviously, other factors must contribute to the development of pain, such as blood supply, neural tension, mechanical deformation, if not many more. We hope that the authors will conduct further studies to help answer this question.

Volker K.H. Sonntag
Phoenix, Arizona
Since the advent of MRI, several papers have been published on the causative relationship between the postdiscectomy peridural fibrosis and recurrent radiculopathy. However, these reports lacked the credibility of a prospective, randomized, blinded study. The present study is indeed a prospective, randomized and double-blinded study of 150 postdiscectomy patients. Thus, the conclusion drawn by the authors that more peridural fibrosis means more postoperative pain, should be regarded as significant and valid. The authors undertook a painstaking methodology that tended to preserve a homogenous patient population and eliminate contamination by too many variables.

While I recognize that the basic thrust of this report was to determine whether peridural fibrosis can cause recurrent radicular pain and if so, whether more fibrosis means more pain, this study raises many new issues and questions that were not discussed or answered herewith. Among these, the overriding issue as I see it would be to identify the possible causes that would result in more fibrosis formation in some patients and less in others. Who is the culprit? The surgeon? The patient? Which elements of the operative technique are most responsible? Is it the extent of bony exposure, which predisposes toward more peridural fibrosis? If so, shouldn't all discectomies be carried out utilizing microsurgical techniques and the operating microscope? To that end, we have established at our institution a clinical pathway for outpatient microdiscectomies. In putting together this prospective protocol, we were very careful, however, in emphasizing the axiom that microsurgical exposure be carried out in accordance with the neurologic presentation and the pathology as demonstrated on the imaging studies. It is wrong to tailor the patient to the operation and cut corners with the exposure. In short, minimum bony exposure (as indicated) will leave the minimum peridural fibrosis. We also feel that the use of the operating microscope is superior to the operating loops in performing the operation with minimum bleeding from the epidural veins, in minimizing retraction and in working in such confined spaces as the nerve root axilla, among others. There are several reasons for this, including the better and changeable magnification with the operative microscope, the much better stereoscopic visualization, especially under high powered magnifications, and the coaxial illumination afforded by the operating microscope.

Furthermore, the issue of the safety and effectiveness of the anti-adhesion barrier gel, ADCON-L, is not resolved satisfactorily enough with this study. I feel confident, though, that we have not heard the last word regarding this and similar substances form the European study group.

Ivan Ciric
Evanston, Illinois

Key words: Lumbar discectomy; MR imaging; Peridural scar; Recurrent radicular pain