



THE IMPORTANCE OF C-REACTIVE PROTEIN IN DISCOGENIC LOW BACK PAIN: THE ANALYSIS OF 444 PATIENTS*

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ABSTRACT

Background: Low back complaint is the most common health problem. Recent studies point out the role of inflammation on discogenic back pain. In this study, we intended to examine the importance of C-reactive protein (CRP) level in discogenic low back pain.

Material and Methods: 444 patients with discogenic low back pain were assessed in three groups. The first group (n=229) consisted of patients who appealed to outpatient clinic and who were recommended medical therapy. In the second group (n=15), there were patients who appealed to outpatient clinic and who were offered operation but who did not accept surgery. As for the third group (n=200) included patients who were operated because of single level lumbar discopathy. All patients were assessed in terms of CRP positivity at the first admission and whether surgery is recommended or not.

Results: Positivity of CRP was significantly higher in the group to whom surgery is recommended (n=215) than in medical treatment recommended patients (17.8 % vs. 3.1 %, p < 0.0001, OR=6.8, 95 % CI: 2.9-15.6). Furthermore, the positivity of CRP was found significantly higher in the third group compared to the first group (18 % vs. 3.1 %, p < 0.0001, OR= 6.9, 95 % CI: 3.1-16.1). However, it was relatively higher in the second group than in the first group (13.3 % vs. 3.1 %, p=0.0626, OR=4.9, 95% CI: 0.9-25.9).

Conclusion: Discogenic low back pain is caused by both mechanical and inflammatory factors. Preoperative CRP values can be predictive for inflammatory process in lomberdiscopathy. For more accurate results further studies are needed.

Key words: C-reactive protein, low back pain, discectomy

Level of Evidence: Retrospective clinical study, Level III.

INTRODUCTION

Low back pain is the second frequent complaint after upper respiratory tract infections in admission to outpatient clinics. It is determined that 80% of all the world's population has complained about low back pain at any time during his/her life ^(1,23,26). The most frequent reason of limitation in motion after 45 years is low back pain. For this reason, low back pain can cause a significant loss of labor in industrialized societies. Since ancient historical times, physicians have been interested in lumbalgia, and at 1909 Fedor Krause ⁽⁶⁾ carried out the first surgical intervention similar to current surgical procedures. Mixer and Barr published surgical series about low back pain at 1934. They emphasized that the most frequent cause of low back pain was lumbar discopathy and the treatment was surgery ^(6,18). After this publication,

surgeons were also interested in discogenic lumbalgia.

Most important reason of mechanical low back pain is the nucleus pulposus degeneration. It is well described that the main pathophysiology of sciatica is related to disc compression to thecal sac and nerve root. However, severe pain without radiologically significant mechanical compression or severe neural compression without lumbosciatica and decreased satisfaction related to pain at postoperative long-term follow up have led the researchers to re-evaluate the pathophysiology ⁽⁵⁾. Clinical and experimental studies in recent years have demonstrated that the inflammation caused by disc content at nerve root may play a significant role in pain mechanism ^(10,17,18). Also, it was clearly shown before that the most important mediators of

neural and epidural inflammation are matrix nitric oxide (NO), metalloproteinase, prostaglandin E2, interleukin (IL)-6 and tumor necrosis factor (TNF)-alpha^(11,28).

In this study, we aimed to examine the importance of C-reactive protein (CRP) levels at discogenic low back pain proceeding to lumbar disc surgery.

MATERIALS AND METHODS

The patients who appealed to our outpatient clinic with low back pain in between January 2012 and July 2012 were inspected retrospectively. Patients who had discogenic low back pain were included to the study. Patients with infectious disease and rheumatologic disease were excluded. All patients were evaluated with magnetic resonance imaging (MRI). Patients having multi-level disc degeneration were excluded from the study. The remaining 244 patients with single level degeneration were evaluated in terms of CRP levels and whether they were recommended surgery or not.

We also retrospectively analyzed another group of the patients who were operated with microdiscectomy for lumbar discopathy during the same time. Two hundred patients aged between 30 and 50 years-old underwent microdiscectomy for single level discopathy. They were the patients who had no additional evidence of infective or rheumatologic disease. Preoperative CRP values of these patients were evaluated for the study.

Statistical Analysis

The MedCalc Software version 10.1.6.0 (Mariakerke, Belgium) was used for analysis. Statistical differences among the groups were identified with *Chi-square* test. In

addition, *odds ratio* (OR) and 95% confidence interval (CI) were determined. P values less than 0.05 were considered as significant.

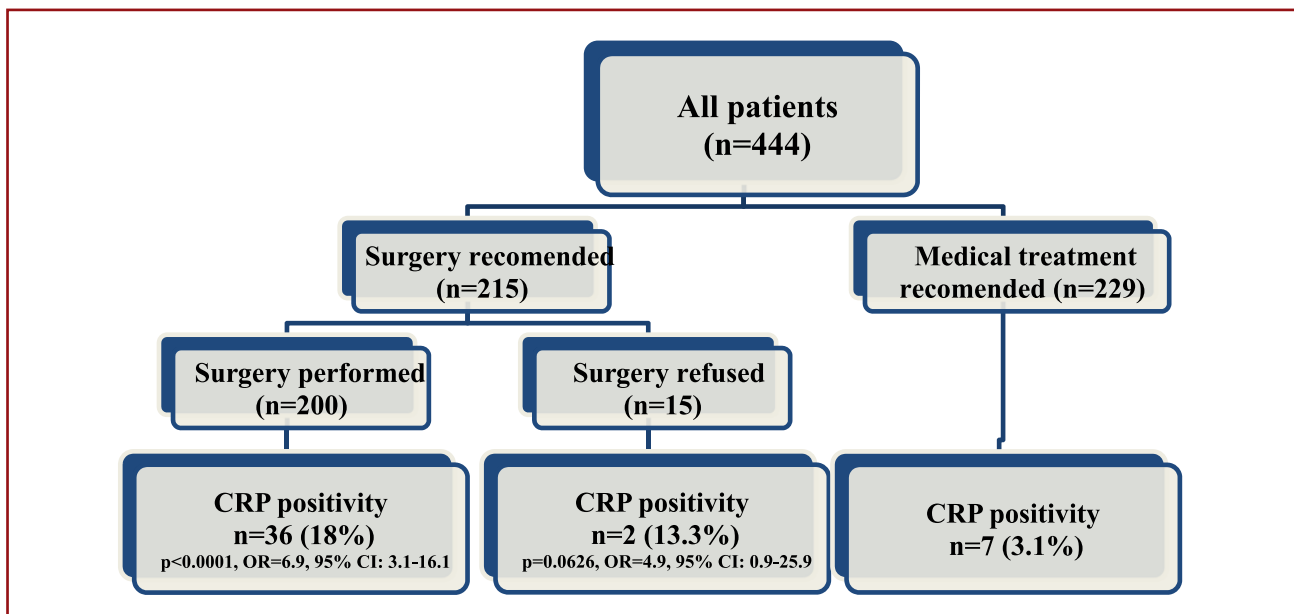
RESULTS

It was seen that surgical intervention was suggested to 15 patients at the evaluation of 244 patients meeting the criteria with discogenic low back pain at our outpatients clinic (Figure-1).

Elevated CRP was detected in 2 of them (13.3%). Also, it was identified that surgery was not recommended to 7 patients having positive CRP levels (3.1%). When these results were examined according to percentage analysis, CRP positivity was seen as 3.7% (n=9) in outpatient clinic's patients. Additionally, CRP positivity was seen at 18% of the operated patients (n=36). The positivity of CRP was significantly higher in the group to whom surgery is recommended (n=215) than in medical treatment recommended patients (17.8% vs. 3.1%, $p < 0.0001$, OR=6.8, 95% CI: 2.9-15.6). Furthermore, the positivity of CRP was found significantly higher in the operated patients compared to the medical treatment recommended patients (18% vs. 3.1%, $p < 0.0001$, OR=6.9, 95% CI: 3.1-16.1). However, it was relatively higher in the patients refused surgery than in the surgery recommended patients (13.3% vs. 3.1%, $p = 0.0626$, OR=4.9, 95% CI: 0.9-25.9) (Figure-1).

When the classification function analysis is considered, the sensitivity and specificity of CRP test at recommendation and performance of surgery is about 17% and 96% respectively. the positive and negative predictive values are founded 84%, 55% (Table-1).

Figure-1. The summary of data



CRP; C-reactive protein, OR; odds ratio, CI; confidence interval

Table-1. The diagnostic performance of C-reactive protein on lumbar disc disease

	Surgery (offered and performed patients) (n=215)	Medical treatment (n=229)
CRP positive (n)	38	7
CRP negative (n)	177	222
Sensitivity		17 %
Specificity		96 %
PPV		84 %
NPV		55 %

CRP; C-reactive protein, PPV; positive predictive value, NPV; negative predictive value

DISCUSSION

Increase in clinical and surgical experience for lumbar discopathy has led the researchers to examine its pathophysiology. After the first identification of lumbar disc herniation in 1930's, the cause of its signs and symptoms was considered as neural compression and this cause was accepted for a long time. However, some debates related to mechanical theory emerged after the development of radiological imaging. Since some clinically apparent herniated lumbar discopathy cases did not show radiologic features despite the presence of severe neural, radicular signs, the probability of another pathophysiologic mechanism besides of mechanical theory is considered⁽¹⁸⁾.

Immune response to disc material was shown and discussed in several articles in 1970's^(3,7-9). However, Guinto et al. were the first to publish a case with spontaneously regressing herniated lumbar disc in clinical interest of this issue⁽⁴⁾. Subsequently, many studies have been published about spontaneous resorption of herniated lumbar disc and have underlined the effect of immunologic response in this process^(2,5,11,27).

The study by Olmarker et al. showed that the placement of autologous nucleus pulposus tissue to sacrococcygeal cauda equina on pigs caused reduction of peripheral nerve conduction and increase of degeneration of root without mechanical pressure⁽²¹⁾. Also, it was shown that this application increases production of substance-p and decreases the threshold of nociceptive receptor⁽¹¹⁾. Intervertebral disc was found to be immunogenic and the development of granulation after epidural injection were observed in similar studies⁽¹⁸⁾. Most of the studies on this issue demonstrated that inflammation was also responsible for radiculopathy and in this situation the most effective content was the nucleus pulposus^(15,16,22,24,30). After the contact of nucleus content with epidural space, releasing of some mediators such as phospholipase A2, prostaglandin E2, IL-1 alpha-beta, IL-6, IL-8, TNF-alpha, NO, granulocyte - macrophage colony - stimulating factor, and triggering of inflammatory response

were shown in studies^(5,10,11,19,24). Some studies demonstrated that after the beginning of the inflammation, migration of macrophages and lymphocytes to epidural space influence the process^(13,14,25,29,30). TNF-alpha was shown to be more forefront in inflammatory radiculopathy formation by most recent studies^(10,18,20).

The release of inflammatory cytokines leads to the increased production of acute phase reactants (APR) by liver in inflammation period. APR are known as indicator of systemic or focal inflammation⁽³⁾.

In our study, we aimed to investigate whether AFR take place or not in inflammatory process and whether they have positivity in surgical cases. In our results, we found higher CRP levels in the samples of patients to whom surgery is recommended when compared to the other group, and also CRP levels were significantly higher in patients who underwent surgery. To avoid incorrect results, we selected the patients who did not have any additional disease or symptoms. For standardization of release of the mediators, patients with one level lumbar disc disease were included to the study. However, correlation is found between this simple blood test and mechanical compression necessitating surgery. This also reflects the correlation between the CRP levels and inflammation cascade in lumbar discopathy. Our surgical indication for lumbar disc disease is basically to remove the mechanical neural compression. Patients who are recommended surgery have much more mechanical neural compression and when CRP values are taken into account in the same group, it is seen that both mechanical and inflammatory processes are involved in lumbar disc herniation.

When the classification function analysis is considered, the sensitivity of CRP test at recommendation and performance of surgery is about 17 %. This indicates that the efficacy of CRP as a screen test in recommendation of surgery is low. But, specificity analysis demonstrates that CRP positivity is a supporting factor of surgical treatment as it is anticipated (96 %). As for the positive and negative predictive values, positive test highly indicates that surgical treatment will be needed.

The main limitation of our study is that the evaluation of CRP was made as positive/negative rather than quantification. Besides, the authors did not provide any radiological parameter such as size of annular tear, volumetric analysis of the fragment, etc. Surely, the study would be more valuable if CRP values were compared with such technical features.

CONCLUSIONS

Preoperative CRP values can be a predictive value for inflammatory process in lumbar discopathy. In discogenic pain, both mechanical compression and inflammation is important. More compression is resulted with more inflammation. For more accurate results, quantitative analysis should be made in the comparison of other cytokines contributing to the inflammatory cascade of lumbar discopathy and CRP, and it should be assessed together with radiological findings.

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