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# ROLE OF HIGH SENSITIVE C-REACTIVE PROTEIN AS A PROGNOSTIC MARKER IN DETERMINING FUNCTIONAL OUTCOME AFTER INTERLAMINAR EPIDURAL STEROID INJECTION IN CERVICAL RADICULOPATHY

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#### Abstract

Background: Local inflammation in the course of a primarily mechanical impingement of a cervical nerve root may be one of the mechanisms causing pain in cervical radiculopathy due to cervical disc herniation. In patients with disc herniation, the level of inflammation varies and by this study we can correlate the functional outcome with pre procedural hs-CRP by which we can come to a conclusion regarding the level or range of hs-CRP at which functional outcome with cervical epidural steroids is better and we can perceive whether hs-CRP can be used as an effective tool for predicting functional outcome after epidural steroids. Materials & Methods: Forty five cases with cervical radiculopathy due to disc herniation (as per criteria by NASS) in the age group of 20-60 years, and on conservative treatment for at-least 4 weeks were enrolled and divided into 2 groups. Baseline demographic data was collected for all patients and physical examination, medical history, surgical history, biplanar radiography and cervical MRI, baseline NDI score and blood sampling to measure baseline hs-CRP from cubital vein were collected. Blood samples were recollected at first month, second month and third month of follow up and hs-CRP and NDI were recorded for all the patients. Results: Mean hs-CRP for cases and controls at baseline was 12±8.281 and 2.42±1.88, respectively and showed statistically significant higher values of hs-CRP in the cases group (p <0.05). There was also a positive correlation found between fall in hs-CRP levels and decrease in NDI scores after administration of CESI, and this correlation was found to be stronger in patients belonging to the acute group rather than the chronic group. Conclusion: Baseline hs-CRP are a useful indicator in patients with cervical radiculopathy to identify the group of patients that will have significant improvement with Cervical Spinal Steroid Injections and thus for ideal selection of patients and avoiding unnecessary intervention for patients with low hs-CRP levels.

# INTRODUCTION

Cervical Epidural Steroid Injections (CESI) have been used for a number of years and have shown intense growth in the treatment of radicular pain of cervical origin after failed conservative management with oral medications, physical therapy and lifestyle modifications. Even World Institute of Pain giving a positive recommendation for interlaminar cervical epidural injections in their 2010 Guidelines for treatment of Cervical Radicular Pain.<sup>[1]</sup> Also, North American Spine Society Review and Recommendation Statement in 2011, has concluded that CESI provide relief in radicular pain in 60-79% of the patients and this relief is maintained for a year

or more. However, it is not common to come across cases who continue to suffer from pain and radicular symptoms even after CESI, becoming a source of confusion amongst the surgeons as well as a cause of despair for the patient and his family. As compared to the earlier notion of herniated disc causing nerve compression, it has become more evident in the previous years that an underlying inflammatory response plays a significant role in radicular symptoms. Prostaglandin E2, Tumor Necrosis Factor alpha (TNF), Interlukein-6 (IL-6), nitric oxide (NO) and matrix metalloproteinases are released by herniated disc, that add to the inflammatory milieu around the nerve roots, aggravating the symptoms. [2-<sup>4]</sup> Thus, we have tried to quantify the extent of inflammation, by using Highly Sensitive C- Reactive Protein (hs-CRP) as a sensitive marker of inflammation. Hs-CRP has been previously used as an indicator for cerebrovascular as well as coronary artery disease, as higher levels predict a high inflammatory milieu, and thus higher risk of thrombosis. The underlying inflammation around herniated discs causes increase in CRP in minute or subclinical levels.<sup>[5]</sup> Steroid injections act by reducing the local inflammation and thus symptomatic improvement for the patients.<sup>[6,7]</sup> With this study, we tried to find a relationship between hs-CRP levels and cervical spine radiculopathy as well as using hs-CRP as a marker to predict the improvement a patient is expected to get after CESI, thus improving the efficacy with which we prescribe these injections and also improve the patient response to CESI.

Approximately 30-50% individuals experience significant neck pain in their lifetime, with point prevalence being 4.9%.<sup>[8]</sup> A population study from Rochester Minnesota found the annual age adjusted incidence of cervical radiculopathy to be 83 per 100,000 persons. The annual incidence was higher for men, and peaked at ages of 50-54 years for both sexes. Either spondylosis or disc protrusions or both were involved in 70% of the cases.<sup>[9]</sup>

"A pain in a radicular pattern in one or both upper extremities related to compression and/or irritation of one or more cervical nerve roots. Frequent signs and symptoms include varying degrees of sensory, motor and reflex changes as well as dysesthesias and paraesthesia's related to nerve root(s) without evidence of spinal cord dysfunction (myelopathy)" is the working definition of cervical radiculopathy as given by North American Spine Society (NASS) in 2010. Foraminal encroachment due to reduced disc height, uncovertebral and zygapophyseal joint degeneration are common causes.<sup>[10]</sup> Herniated discs are less common causes, unlike lumbar spine where herniated disc are the main reason of symptoms

The arm pain typically follows a myotomal pattern, whereas the sensory symptoms such as burning and tingling follow a dermatomal distribution. Cervical radicular pain is often described as the pain perceived by the patient in the upper extremity caused by irritation and / or injury of a cervical spinal nerve, whereas cervical radiculopathy in addition to radicular pain also includes neurologic signs such as motor or sensory changes. Thus, cervical radicular pain and cervical radiculopathy may be caused by the same clinical entities and they may present simultaneously, radiculopathy may advance from initial radicular pain when the underlying disorder progresses and both these descriptions have been used interchangeably among patients. The exact pathogenesis of radicular pain still remains unclear, it is thought that compression alone may not always be enough to cause pain, and that an inflammatory chemical component is often required. It has been found that various chemical mediators involved in the inflammatory process are released from sensory neurons and intervertebral disc tissues, contributing to the occurrence of pain.<sup>[11]</sup> Also increased permeability of membrane of dorsal root ganglion is also hypothesized as a source of radicular pain.<sup>[12,13]</sup> Compromise of the neural foramen leading to impingement of the exiting nerve root may result in impairment of the blood supply to the nerve itself. Radicular arteries present within the dural root sleeve as well as the venous flow may be inhibited, causing spasm and ultimately decreased perfusion to the nerve.

Initial treatment is conservative with pain relief medications, physical therapy or a cervical orthosis. If no improvement after three to four weeks of conservative management, then the patients are considered for CESI. Surgical, usually is considered the last resort and is reserved for patients who continue to have persistent and disabling pain even after 6 to 12 weeks of conservative management, progression of neurological deficits, or signs of moderate to severe myelopathy.

CESI have now been used for almost a decade for treatment if radicular pain, due to multitude of reasons, mostly secondary to post cervical surgery syndrome.<sup>[14,15]</sup> CESI can be administered intralaminar or transforaminal, with fluoroscopyguided intralaminar being the preferred and studied approach of the two.<sup>[16]</sup> The local infiltration of steroid is thought to have an anti-inflammatory action. primarily by reducing levels of Phospholipase-A2, but also have action on cellmediated activity and cytokines which add to the inflammation around the nerve roots. In addition to their anti-inflammatory effects, steroids inhibit pain by suppressing ectopic discharges from injured nerve fibres and also inhibit conduction in the normal unmyelinated C fibers.<sup>[5]</sup> The addition of local anaesthetic can increase blood flow to the nerve roots as well as stifle ectopic discharges emanating from injured neurons as well as slow down or even interrupt the nociceptive transmission.[17,18]

The benefits of cervical ESIs remain difficult to quantify because of the paucity of randomized trials of sufficient sample size. Small prospective and retrospective observational studies have suggested that either transforaminal or interlaminar ESIs can provide benefits for up to six months or longer in 40% to 84% of patients, <sup>[6,19]</sup> evidence been derived from controlled randomized trials. Diwan *et al*<sup>[20]</sup>, in a systematic review, identified 13 studies, utilizing 4 randomized trials assessing cervical disc herniation, meeting inclusion criteria for methodological quality assessment. Based on this review, they concluded that for cervical disc herniation, there is good evidence for cervical epidural with local anaesthetics

and steroids, whereas the evidence is fair with local anaesthetics only.

Local inflammation is a definite culprit in the radicular symptoms experienced by the patients, and CRP is one of the first markers of systemic inflammation which can be measured by laboratory tests, appearing within 6 to 8 hours after infection.

Local inflammation in the course of a primarily mechanical impingement of a cervical nerve root may be one of the mechanisms causing pain in cervical radiculopathy due to cervical disc herniation. The cytokines that are produced during and also participate in the inflammatory processes are the chief stimulators for liver cells to synthesize a wide array of acute phase proteins including CRP.<sup>[2,3]</sup> Recently ultrasensitive methods of assaying serum CRP levels have been developed and used which allow to detect and express CRP in subclinical ranges, as high sensitive CRP, hs-CRP assessed with these methods has been contemplated to be an independent predictor of the incidence of cardiovascular diseases such as stroke or myocardial infarction. It is however crucial, that factors with potential influence on hsCRP such as alcohol<sup>[21]</sup>, smoking<sup>[22]</sup>, body mass index (BMI)<sup>[22]</sup>, physical activity and medications<sup>[21]</sup> are taken into account, since they can influence the CRP levels.

CRP as an acute phase reactant is one of the most sensitive and most widely used parameters especially when evaluating the course of local and systemic inflammation, especially CRP levels detected with ultrasensitive assays have shown that even subclinical ranges of CRP (<5mg/dl) which were considered normal earlier have a strong correlation with cardiovascular risk.<sup>[23]</sup> No consensus about the relation of hs-CRP and lower back ache came out of this literature search with some studies showing positive correlations between pain and outcomes of ESI whereas others showing no correlation. To our knowledge, this study is the first to evaluate the usefulness of hs-CRP as a prognostic marker for predicting the efficacy of cervical interlaminar epidural steroid injection in patients with cervical radiculopathy due to disc herniation. In addition the purpose of this study is to evaluate the clinical relevance of hs-CRP in patients with cervical radiculopathy due to disc herniation in subclinical ranges as it has been shown for patients with cardiovascular disease. In our study we used preprocedural hs-CRP levels which are often raised in patients of cervical radiculopathy due to disc herniation with predominant inflammation. These patients were given epidural steroid injections which caused this local inflammation to settle down.

In patients with disc herniation, the level of inflammation varies and by this study we can correlate the functional outcome with pre procedural hs-CRP by which we can come to a conclusion regarding the level or range of hs-CRP at which functional outcome with cervical epidural steroids is better and we can perceive whether hs-CRP can be used as an effective tool for predicting functional outcome after epidural steroids.

#### **MATERIALS AND METHODS**

The study was approved by the ethics committee at our institution. Informed and written consent was obtained from all the participants before enrolment in the study.

Our population of interest consisted of patients with cervical radiculopathy due to disc herniation attending the Orthopaedics out-patient department at PGIMER, Chandigarh. Forty five cases with cervical radiculopathy due to disc herniation (as per criteria by NASS) in the age group of 20-60 years, and on conservative treatment for at-least 4 weeks were enrolled and divided into 2 groups as shown below [Figure 1].





#### **Inclusion Criterion**

- 1. Age between 20 to 60 yrs.
- 2. Patients fulfilling the criteria for cervical radiculopathy as laid down by NASS (2010).
- 3. Clinical evidence of herniation in the form of disc related radicular pain of more than four weeks duration interfering with daily activities.
- 4. Failure to respond to conservative treatment modalities including physical therapy, a structured exercise program and drug therapy.
- 5. Radiological evidence of disc herniation on MRI cervical spine.
- 6. Patients competent to understand the study protocol, provide voluntary written informed consent, and participate in outcome measures.

Baseline demographic data was collected for all patients and physical examination, medical history, surgical history, biplanar radiography and cervical MRI, baseline NDI score and blood sampling to measure baseline hs-CRP from cubital vein were collected.

#### **Exclusion Criterion**

1. Patients who have chronic inflammatory disease or malignancy.

- 2. Patients having any local or systemic source of infection.
- 3. Patients with ischemic heart disease and history of stroke.
- 4. Patients suffering from diabetes\
- 5. Patients with history of smoking.
- 6. Patients with history of chronic alcoholism.
- 7. Patients with high body mass index (BMI>25).
- 8. Patients on statins, corticosteroids, ACE inhibitors, anti-platelets and beta blockers.
- 9. Patients with history of cervical spine surgery and radiculitis secondary to spinal stenosis.
- 10. Patients with discogenic pain without disc herniation.
- 11. Patients with history of any major surgical procedure in the past one year.
- 12. Patients suffering from Psychiatric disorders.
- 13. Any condition that could interfere with the interpretation of the outcome and assessment such as pregnancy, lactation or a history of adverse reactions tosteroids.
- 14. Patients with body temperature more than 99 degree Fahrenheit at presentation.
- 15. Patients showing signs and symptoms of any acute inflammatory disease during the study were withdrawn from the study.

More severe the disc disease more will be the NDI score. The NDI is a simple, reliable, valid, sensitive and specific assessment and it can be used in patients with cervical radiculopathy. The NDI has sufficient support and usefulness to retain its current status as the most commonly used self-report measure for neck pain. Baseline NDI and hs-CRP values were measured and a single CESI was given to all our cases, administered by a single anesthetist via intralaminar approach.

A decrease in NDI score of 10 or more was considered significant for analysis purpose post CESIs. Blood samples were recollected at first month, second month and third month of follow up and hs-CRP and NDI were recorded for all the patients. All blood samples were analyzed to assess the hsCRP concentration, as measured by a solid phase enzyme immunoassay. We have used the C-Reactive Protein Ultra-Sensitive Elisa Kit, a product of XemaCo., Ltd. in our study.

#### **Statistical Analysis**

The data was entered using Microsoft Excel 2007 and analyzed using SPSS (statistical package for the social sciences) software version 17.0. After establishing normality of data, unpaired t-test was used to compare means of hs-CRP of two groups, and chi-square test was used for comparison of proportions between groups, namely acute and chronic groups NDI scores. ANOVA was used to find trends of hs-CRP and NDI scores in acute and chronic cases and in group 1 and 2. Pearsons correlation coefficient was used for determining correlation between decrease in hs-CRP levels and falling NDI scores post CESI.

#### RESULTS

There were 45 patients taken as cases and 41 patients in control group. Mean age among cases was 42.93, whereas the mean age among controls was 42. Group 1 had 15 males and 18 female patients whereas group 2 had 5 male and 7 female patients. Among the control group there were 21 males and 20 female patients. Mean BMI for case and control group was  $22.32\pm2.021$  and  $22.20\pm2.015$ , respectively. Mean hs-CRP for cases and controls at baseline was  $12\pm8.281$  and  $2.42\pm1.88$ , respectively and showed statistically significant higher values of hs-CRP in the cases group (p <0.05) [Figure 2].

Furthermore, baseline hs-CRP in patients with acute and chronic symptoms was  $6.926\pm6.926$  and  $17.17\pm9.750$ , respectively showing a statistically significant higher values in chronic cases (p<0.05) (Figure 3). Among the 45 cases, there were 30 cases of single level and 15 cases of multi-level cases with mean hs-CRP being  $12.69\pm6.92$  and  $11.69\pm7.55$ , respectively and did not show any statistical significance with hs-CRP levels or with intensity of pain(p > 0.05) [Figure 4].

Mean hs-CRP at presentation among cases with significant reduction in NDI (>10 points) after administration of CESI was 12.71±7.008 as compared to 5.592±3.879 baseline values for those with insignificant changes in NDI. Thus, CESI is more effective in patients with higher baseline hs-CRP. Also, group 1 showed greater reduction in hs-CRP as compared to group 2 and the fall was more significant during the first month after the injection as compared to subsequent months [Figure 5].

There was also a positive correlation found between fall in hs-CRP levels and decrease in NDI scores after administration of CESI, and this correlation was found to be stronger in patients belonging to the acute group rather than the chronic group [Figure 6].



Figure 2: Box plot showing baseline hs-CRP in case and control groups



Figure 4: hs-CRP levels in patients with significant and insignificant fall in post-CESI NDI score



Figure 5: Trend of hs-CRP values in patients with significant reduction in NDI scores and patients with insignificant reduction in NDI scores in acute cases

Table 1. Studies relating its CAT with fumbal disc disease							
Author	hsCRP	ESI	Low	Cervical	Sample	Level of	Result
	used as		backache	radiculopathy	size	evidence	
Benoy V et al (2014) <sup>[24]</sup>	Predictor of outcome	Used	+	-	50 articles	Systematic review	No significant relation
Park et al (2011) <sup>[25]</sup>	Predictor of VAS	Used	+	-	55	Case series	No correlation
Ackerman et al $(2006)^{[26]}$	Predictor of outcome	Used	+	-	60	Case- Control	Negative correlation
Sugimori et al (2003) <sup>[27]</sup>	Predictor of outcome	Used	+	-	101	Case- Control	Negative correlation
Le Gars et al (2000) <sup>[28]</sup>	Predictor of symptoms	Used	+	-	70	Case- Control	Positive correlation
Gebhardt et al (2006) <sup>[29]</sup>	Predictor of outcome	Used	+	-	72	Case series	Negative correlation
Stürmer et al (2005) <sup>[30]</sup>	Predictor of VAS	Used	+	-	72	Prospective case series	Positive with Acute/Negative With chronic symptoms

#### Table 1: Studies relating hs-CRP with lumbar disc disease

## DISCUSSION

Cervical radiculopathy can be a troublesome disease for the patient because of the discomfort it causes as well as for the orthopedician due to the limited number of treatment options and protracted response to these treatment modalities. It is a common practice to advice patients with cervical radiculopathy to opt

# Figure 3: Box plot showing baseline hs-CRP levels between acute, chronic and control groups





for Cervical Epidural Steroid injection (CESI) after exhaustion of conservative management like analgesics, muscle relaxants, rest and physiotherapy. But, now it has become common ground to find multiple patients with continued symptoms and pain even after epidural steroid injections. Furthermore, it is often found that patients who respond well as well as those who do not respond well to CESI, have similar MRI findings. This signifies that it is not only the mechanical compression of the nerve roots, but also the inflammation around the nerve roots, which plays an active role in the pain perceived by the patient. Epidural steroids act on this inflammatory component of pain and help to reduce the ongoing symptoms. A comprehensive literature search did not reveal any study to prognosticate or differentiate group of patients who would show a satisfactory response to epidural steroids from those who elicit an unsatisfactory response. We in our study have tried to focus on this issue and used hs-CRP, which can be used as a prognostic marker to differentiate and give cervical epidural steroids to patients who are more likely to respond satisfactorily rather than prescribing epidural steroids to every patient with persistent cervical radiculopathy not responding to conventional treatment. Also, we tried to evaluate clinical relevance of hs-CRP in patients with cervical radiculopathy, in subclinical ranges as it has been shown for cardiovascular diseases.

There is a dearth of studies which explore the relation between CRP levels and cervical radiculopathy or using CRP as a predictor of response to CESI, though multiple studies have been published exploring the relation between hs-CRP and lower back ache.

Cervical epidural steroid injections have been studied since 1985. Historically, cervical epidural steroid injections originated from Pages description of needle placement into the lumbar epidural space based on obstruction of free flow of spinal fluid from the needle and lack of resistance to injection of local anaesthetic in 1921.<sup>[31]</sup>

Benyamin el al.<sup>[32]</sup> in a systematic review of the effectiveness of cervical epidurals in the management of chronic neck pain, illustrated moderate evidence for cervical epidurals in the management of chronic neck and upper extremity pain. Manchikanti et al.[19], in a comprehensive assessment of the literature for ASIPP guidelines, concluded that evidence for the effectiveness of cervical interlaminar epidural injections is good for radiculitis secondary to disc herniation, whereas it is fair for pain of central spinal stenosis. Among the randomized trials Castagnera et al<sup>33</sup>, included 24 patients in their study and reported a success rate of 78.5% in the steroid group. Stav et al<sup>[34]</sup>, had 42 patients in their study and good pain relief was reported in 76% of the patients. The study by Pasqualucci et al.<sup>[35]</sup>, consisted of 40 patients and they achieved a pain control of 80% in the patients. Laxmaiah Manchikantet et al.<sup>[19]</sup>, in their studies reported significant pain relief in 82% in a study consisting of 120 patients and 87% in a trial with 60 patients respectively. Lee.<sup>[25]</sup> performed a prospective

outcome study on 98 patients with cervical radiculopathy and showed that 80% patients avoided surgery because of better pain relief.

We in our study administered fluoroscopically guided interlaminar cervical epidural injection to 45 patients. 37 patients showed good functional outcome as determined by the neck disability index whereas there were 8 patients in our study with no pain relief or even worsening of pain after epidural steroid injection. We in our study achieved 82% success rate in pain relief and improved functional outcome.

No literature was found relating the hs-CRP levels to the cervical radiculopathy symptoms or elucidating the effects of pre procedural hs-CRP on results of CESI or discectomy surgery. Most of the studies in literature, explored a relation between hs-CRP and lumbar disc disease. These studies used Visual Analogue Scoring as an outcome parameter, nephlometric assay for measuring hs-CRP levels, and unmatched control groups in terms of age, sex and BMI. We used turbidimetric assay for measurement of serum hs-CRP levels, NDI score for pain assessment which is more sensitive, specific and reliable than VAS, and we also had strict exclusion criterion to ensure that the case and control groups are matched.

We found that there was a significant elevation in baseline hs-CRP in patients with cervical radiculopathy, irrespective of acute or chronic nature of symptoms, as compared to the levels in control group. On three months follow up it was noticed, that there was a significant fall in hs-CRP levels and pain and a corresponding improvement in functional outcome as measured by NDI score in the patients with acute symptoms, where-as the levels were more or less constant as well as functional improvement was much less in chronic cases as compared to acute cases. Also, we found that patients in group 1, with higher baseline hs-CRP responded better to CESI as assessed by NDI score as compared to group 2 patients, who had a lower baseline hs-CRP. The increase in baseline hs-CRP in acute cases is expected due to the inflammatory component involved. Chronic pain in cervical radiculopathy can be multifactorial in origin, involving a larger component of non-inflammatory pathology or a mechanical pathology, and this can be a possible reason for our findings.

One of the contrasting findings, was the higher levels of hs-CRP in all chronic cases as compared to baseline levels in acute cases, one of the factors explaining this is that chronic disease involves ongoing and recurring inflammation around the nerve roots, which can explain the higher hs-CRP levels. Another reason can be a confounding factor which is causing an inflammatory milieu and spuriously giving higher hs-CRP readings, for which we established and implemented very strict inclusion and exclusion criterion to ensure any source of chronic inflammation like local or systemic infections, diabetics, smokers, alcoholics, obese or underweight patients, patients with history of drug intake or recent surgery, to be excluded from our sample as well as control group.

Even previous studies by Sugimori et al.<sup>[27]</sup> and Le Gars et al<sup>[28]</sup> have shown there is no relation between level or number of disc herniation and baseline hs-CRP levels for lumbar spine disease, and the same results were replicated in our study for cervical spine. Thus, the level of disc disease is independent of baseline hs-CRP levels and that single level or multiple level disc disease do not have any bearing on pain or discomfort felt by the patient.

In both the groups, greater the baseline hs-CRP, greater was the relief as assessed by NDI. Thus, pain relief was better in group 1 (hs-CRP >5) than in group 2 (hs-CRP < 5). Studies by Rathod et al.<sup>[36]</sup>, Sugimori et al<sup>27</sup> and Le Gars et al.<sup>[28]</sup> elucidate the relationship between pre procedural and post-surgical( discectomy ) hs-CRP levels in lumbar spine disease. All three studies found a significant correlation between pre-op hs-CRP and post-operative pain scores. They concluded that patients with higher preop hs-CRP are prone to have insignificant results after surgery, the reason being that pain in patients with higher hs-CRP is primarily due to multiple inflammatory reasons rather than primarily being mechanical, and thus pain doesn't improve with discectomy. Thus, hs-CRP can act as a good supplementary prognostic marker for operative decision making in borderline and troublesome cases of radicular pain. Thus, risk stratification using preoperative hs-CRP levels can help the patient as well as the doctor to be informed about the likely results of any procedure done on these patients.

In our study we studied the correlation between preprocedural hs-CRP levels and post procedural (CESI) pain scores. We used enzyme linked immunosorbent assay to measure hs-CRP and NDI score for pain intensity before and after the procedure and then on follow- up in first, second and third month. We found that there is a significant correlation between baseline serum hs-CRP levels at presentation and the success of Cervical epidural steroid injections, with the conclusion that serum hs-CRP can be used as a prognostic marker in cases of cervical radiculopathy and also a prognostic marker in patient selection for surgery. We can use hs-CRP levels in patients with cervical radiculopathy in subclinical ranges as it has been shown for patients with cardiovascular disease. Patients with cervical radiculopathy can be divided into subclinical groups like we did in our study. Patients in Group 1 with high baseline hs-CRP at presentation showed good response to CESI, whereas patients in Group 2 with low baseline hs-CRP values showed a poor response and such patients will be better candidates for surgery as their pathology is primarily mechanical. Similarly patients in Group 1 will be poor candidates for surgery since their primary pathology is an inflammatory reaction around the nerve roots. This can be helpful for the clinician to make informed decision about what procedure would provide better relied for which patient, and no such criterion is present at the moment to classify patients with cervical radiculopathy at present. To conclude hs-CRP levels can also be used as a supplementary prognostic marker for operative decision making in troublesome and borderline cases of cervical radiculopathy as well as to identify the primary cause of symptoms in patients with cervical radiculopathy.

### CONCLUSION

Baseline hs-CRP are an useful indicator in patients with cervical radiculopathy to identify the group of patients that will have significant improvement with Cervical Spinal Steroid Injections and thus for ideal selection of patients and avoiding unnecessary intervention for patients with low hs-CRP levels. Thus, all patients suspected to have cervical radiculopathy should undergo baseline hs-CRP evaluation to ensure if they are good candidates for CESI or they might need other modalities of treatment.

#### REFERENCES

- Van Zundert J, Huntoon M, Patijn J, Lataster A, Mekhail N, van Kleef M, et al. 4. Cervical Radicular Pain. Pain Pract. 2010 Jan;10(1):1–17.
- Saal JS, Franson RC, Dobrow R, Saal JA, White AH, Goldthwaite N. High levels of inflammatory phospholipase A2 activity in lumbar disc herniations. Spine (Phila Pa 1976). 1990 Jul;15(7):674–8.
- Grönblad M, Virri J, Tolonen J, Seitsalo S, Kääpä E, Kankare J, et al. A controlled immunohistochemical study of inflammatory cells in disc herniation tissue. Spine (Phila Pa 1976). 1994 Dec 15;19(24):2744–51.
- Matsui Y, Maeda M, Nakagami W, Iwata H. The involvement of matrix metalloproteinases and inflammation in lumbar disc herniation. Spine (Phila Pa 1976). 1998 Apr 15;23(8):863–8; discussion 868-9.
- Kang JD, Georgescu HI, McIntyre-Larkin L, Stefanovic-Racic M, Donaldson WF, Evans CH. Herniated lumbar intervertebral discs spontaneously produce matrix metalloproteinases, nitric oxide, interleukin-6, and prostaglandin E2. Spine (Phila Pa 1976). 1996 Feb 1;21(3):271–7.
- Slipman CW, Lipetz JS, Jackson HB, Rogers DP, Vresilovic EJ. Therapeutic selective nerve root block in the nonsurgical treatment of atraumatic cervical spondylotic radicular pain: a retrospective analysis with independent clinical review. Arch Phys Med Rehabil. 2000 Jun;81(6):741–6.
- Carragee EJ, Hurwitz EL, Cheng I, Carroll LJ, Nordin M, Guzman J, et al. Treatment of Neck Pain. Spine (Phila Pa 1976). 2008 Feb 15;33(Supplement):S153–69.
- Hogg-Johnson S, van der Velde G, Carroll LJ, Holm LW, Cassidy JD, Guzman J, et al. The Burden and Determinants of Neck Pain in the General Population. Spine (Phila Pa 1976). 2008 Feb 15;33(Supplement):S39–51.
- Radhakrishnan K, Litchy WJ, O'Fallon WM, Kurland LT. Epidemiology of cervical radiculopathy. Brain. 1994 Apr;117(2):325–35.
- Balasubramanian C, Price R, Brydon H. Anterior Cervical Microforaminotomy for Cervical Radiculopathy – Results and Review. min - Minim Invasive Neurosurg. 2008 Oct 14;51(05):258–62.
- Rao R. Neck Pain, Cervical Radiculopathy, and Cervical Myelopathy. J Bone Jt Surgery-American Vol. 2002 Oct;84(10):1872–81.

- Manifold SG, McCann PD. Cervical radiculitis and shoulder disorders. Clin Orthop Relat Res. 1999 Nov;(368):105–13.
- Cooper RG, Freemont AJ, Hoyland JA, Jenkins JP, West CG, Illingworth KJ, et al. Herniated intervertebral discassociated periradicular fibrosis and vascular abnormalities occur without inflammatory cell infiltration. Spine (Phila Pa 1976). 1995 Mar 1;20(5):591–8.
- Candido KD, Knezevic N 'Nick.' Cervical Epidural Steroid Injections for the Treatment of Cervical Spinal (Neck) Pain. Curr Pain Headache Rep. 2013 Feb 12;17(2):314.
- Manchikanti L, Cash KA, Pampati V, Malla Y. Fluoroscopic cervical epidural injections in chronic axial or disc-related neck pain without disc herniation, facet joint pain, or radiculitis. J Pain Res. 2012 Jul;5:227.
- Beyaz SG, Eman A. Fluoroscopy guided cervical interlaminar steroid injections in patients with cervical pain syndromes: a retrospective study. J Back Musculoskelet Rehabil. 2013;26(1):85–91.\
- Yabuki S, Kikuchi S. Nerve root infiltration and sympathetic block. An experimental study of intraradicular blood flow. Spine (Phila Pa 1976). 1995 Apr 15;20(8):901– 6
- Helm Ii S, Benyamin RM, Chopra P, Deer TR, Justiz R. Percutaneous adhesiolysis in the management of chronic low back pain in post lumbar surgery syndrome and spinal stenosis: a systematic review. Pain Physician. 15(4):E435-62.
- Manchikanti L, Cash KA, Pampati V, Wargo BW, Malla Y. The effectiveness of fluoroscopic cervical interlaminar epidural injections in managing chronic cervical disc herniation and radiculitis: preliminary results of a randomized, double-blind, controlled trial. Pain Physician. 13(3):223–36.
- Diwan S, Manchikanti L, Benyamin RM, Bryce DA, Geffert S, Hameed H, et al. Effectiveness of cervical epidural injections in the management of chronic neck and upper extremity pain. Pain Physician. 15(4):E405-34.
- Imhof A, Froehlich M, Brenner H, Boeing H, Pepys MB, Koenig W. Effect of alcohol consumption on systemic markers of inflammation. Lancet. 2001 Mar 10;357(9258):763–7.
- Rohde LE, Hennekens CH, Ridker PM. Survey of Creactive protein and cardiovascular risk factors in apparently healthy men. Am J Cardiol. 1999 Nov 1;84(9):1018–22.
- Bassuk SS, Rifai N, Ridker PM. High-sensitivity C-reactive protein: clinical importance. Curr Probl Cardiol. 2004 Aug;29(8):439–93.
- Benny B V, Patel MY. Predicting epidural steroid injections with laboratory markers and imaging techniques. Spine J. 2014 Oct 1;14(10):2500–8.

- Park CH, Lee SH. Prognostic Usefulness of High Sensitivity C-Reactive Protein for Transforaminal Epidural Steroid Injection in Patients with Radicular Pain. Pain Med. 2011 Feb 1;12(2):219–23.
- Ackerman WE, Zhang J-M. Serum hs-CRP as a useful marker for predicting the efficacy of lumbar epidural steroid injections on pain relief in patients with lumbar disc herniations. J Ky Med Assoc. 2006 Jul;104(7):295–9.
- Sugimori K, Kawaguchi Y, Morita M, Kitajima I, Kimura T. High-sensitivity analysis of serum C-reactive protein in young patients with lumbar disc herniation. J Bone Joint Surg Br. 2003 Nov;85(8):1151–4.
- Le Gars L, Borderie D, Kaplan G, Berenbaum F. Systemic inflammatory response with plasma C-reactive protein elevation in disk-related lumbosciatic syndrome. Joint Bone Spine. 2000;67(5):452–5.
- 29. Gebhardt K, Brenner H, Stürmer T, Raum E, Richter W, Schiltenwolf M, et al. The course of high-sensitive Creactive protein in correlation with pain and clinical function in patients with acute lumbosciatic pain and chronic low back pain-A 6 months prospective longitudinal study. Eur J Pain. 2006 Nov;10(8):711–711.
- Sturmer T, Raum E, Buchner M, Gebhardt K, Schiltenwolf M, Richter W, et al. Pain and high sensitivity C reactive protein in patients with chronic low back pain and acute sciatic pain. Ann Rheum Dis. 2005 Jun 1;64(6):921–5.
- Dogliotti AM. Segmental peridural spinal anesthesia. Am J Surg. 1933 Apr 1;20(1):107-18.
- Benyamin RM1, Singh V, Parr AT, Conn A, Diwan S AS. Systematic review of the effectiveness of cervical epidurals in the management of chronic neck pain. - PubMed- NCBI [Internet]. Pain Physician. 2009 [cited 2019 Jun 23]. p. 12(1):137-57. Available from: https://www.ncbi.nlm.nih.gov/pubmed/19165300
- Castagnera L, Maurette P, Pointillart V, Vital JM, Erny P, Sénégas J. Long-term results of cervical epidural steroid injection with and without morphine in chronic cervical radicular pain. Pain. 1994 Aug;58(2):239–43.
- Stav A, Ovadia L, Sternberg A, Kaadan M, Weksler N. Cervical epidural steroid injection for cervicobrachialgia. Acta Anaesthesiol Scand. 1993 Aug;37(6):562–6.
- 35. Pasqualucci A, Varrassi G, Braschi A, Peduto VA, Brunelli A, Marinangeli F, et al. Epidural Local Anesthetic Plus Corticosteroid for the Treatment of Cervical Brachial Radicular Pain: Single Injection Versus Continuous Infusion. Clin J Pain. 2007 Sep;23(7):551–7.
- Rathod T, Ladkat K, Chavan S, Chavan A, Chandanwale A, Bhosale P. High sensitive C- reactive protein-Effective tool in determining postoperative recovery in lumbar disc disease. Indian J Orthop. 2014 Jul;48(4):354.