International Journal of Science and Research (IJSR)
ISSN: 2319-7064
Impact Factor 2024: 7.101

Triple Interventional Approach for the Comprehensive Management of Cervical Pain, Secondary to Discal and Facet Joint Pathology

Rafael Orlando Vallejo Estrella[1], Francisco Javier Machuca Vigil[2], Roberto Jameson Rosales[3], Alan Gabriel Martínez Castro[4], Francesca Dolciami[5]

[1, 2]Anesthesiologist, Pain Medicine Physician, Fellow of Interventional Pain Practice, Dolomedic Alta Especialidad en Manejo del Dolor, H. Matamoros, Tamaulipas, México.
Corresponding Author Email: *doc_orlo[at]hotmail.com*

[3]Anesthesiologist, Pain Medicine Physician, Dolomedic Alta Especialidad en Manejo del Dolor, H. Matamoros, Tamaulipas, México.

[4]Trauma / Orthopedic Surgeon, Spine Surgeon, Dolomedic Alta Especialidad en Manejo del Dolor, H. Matamoros, Tamaulipas, México.

[5]Medical Doctor, Dolomedic Alta Especialidad en Manejo del Dolor, H. Matamoros, Tamaulipas, México.

Abstract: ***Cervical pain is a prevalent condition affecting 60% to 70% of individuals at some point in life. This study examines a triple interventional approach for the comprehensive management of cervical pain secondary to discal and facet joint pathology. A total of 16 patients with grade I and II cervical hernias underwent three interventional treatments: thermal intradiscal radiofrequency, zygapophyseal joint denervation, and epidural steroid injection. Follow-up assessments at 1, 3, and 6 months showed a significant reduction in pain, with a mean NRS score decreasing from 6.5 to 1.9. The findings suggest that this approach may serve as an effective alternative between conservative pharmacological treatments and surgical interventions. Further studies with larger sample sizes are required to validate these results.***

Keywords: Cervical pain, interventional approach, discogenic pain, radiculopathy

1. Introduction

Discogenic pain is defined as pain originating from the intervertebral disc. This pain is non-radicular in nature and can occur even in the absence of spinal deformities in the cervical, thoracic, or lumbar segments.[1 2] Despite the presence of an intervertebral disc with its posterior annulus showing no apparent changes in its outer border, it is now accepted that multiple changes or processes (such as annular tears, degeneration, endplate injury, inflammation.) can stimulate the proliferation and potential sensitization of nociceptors in the intervertebral disc, regardless of whether or not the nerve root exhibits symptoms.

In 1947, Inman and Saunders first introduced the concept of discogenic pain.[3] The term was first used in 1969 by Fernstrom, and in 1970, Crock was the first to study the mechanism of discogenic pain. He ultimately defined the term *internal disc disruption (IDD)*, which was attributed to low back pain lasting more than four months and not responding to conservative treatment but that could also be reproduced with provocative discography.[4]

Cervical and lumbar pain reflect complex diseases (where "disease" is defined as any impairment of the normal physiological function of an organ or body part).[5] Although the existence of intervertebral disc innervation and, consequently, the concept of the intervertebral disc as a primary source of back or neck pain were initially controversial, they are now well documented and form an important foundation for current cervical and lumbar pain management practices.[6 7 8]

It is important to remember a key statement from the 1988 publications by Bogduk, Windsor, and Inglis: "These anatomical findings (e.g., cervical nerves and sinuvertebral nerves supplying the disc) provide the previously missing substrate for primary disc pain and pain induced by provocative discography.[9]

Epidemiology

The epidemiology of cervical pain is of impressive magnitude, with an estimated 60% to 70% of the population expected to experience cervical pain at some point in life. The annual prevalence of frequent or persistent neck pain ranges from 2% to 11%.[10 11] In a survey conducted in the United States in 2008, 14% of the adult population reported experiencing neck pain within the three months prior to the survey.[10] Cervical discogenic pain is estimated to be the most common cause of persistent neck pain, affecting between 16% and 41% of patients.[12]

Etiology

The etiology of discogenic pain is as complex as the network of nerves surrounding it. The sensory innervation of the intervertebral disc involves branches of the sinuvertebral nerve, the main anterior branch, the gray ramus, and the sympathetic chain. This confirms that the intervertebral disc can be a source of pain and has the potential to generate autonomic reflexes.

For many years, it was believed that the nucleus, inner annulus, and middle annulus were completely avascular and aneural. Nerve fibers were thought to be present only in the outer portion of the posterior and anterolateral annulus, making these regions the primary sources of discogenic pain.

Today, pain conducting nerve fibers can be present in the middle annulus and, in some cases, even reach the nucleus pulposus. This has been observed both in degenerative discs and in cases of discogenic back pain, which suggests that this phenomenon can occur at any spinal level, including the cervical region.[13]

Studies have shown that up to 77% of discs surgically removed due to discogenic pain, confirmed via discography, exhibit nerve fiber growth into the middle third of the annulus fibrosus. In contrast, only 6% of control group discs show this internal nerve fiber growth pattern. Additionally, these pain related nerve fibers have been associated with the presence of substance P, an active neurotransmitter in pain transmission.[14] [15]

Similarly, numerous mechanoreceptors and pain-producing neurons have been clinically and experimentally identified in the discs of patients with chronic discogenic pain.[16] [17] [18] This evidence leads to the conclusion that the etiology of discogenic pain is highly complex, influenced by somatosensory and autonomic innervation, peripheral sensitization, and amplification mechanisms that impact pain perception. In many cases, this pain presents characteristics like visceral pain, despite originating from a clear musculoskeletal structure.[19]

Physiology of the intervertebral disc

In the lumbar region, the disc is approximately 7 to 10 mm thick and 4 cm in diameter and consists of three regions: the nucleus pulposus, the annulus fibrosus, and the endplate.[20] The vertebral endplate is considered more a part of the intervertebral disc than of the vertebral body, as it is not directly attached to the subchondral bone of the vertebrae but rather interwoven into the annulus of the intervertebral disc.[21]

The nucleus pulposus is normally avascular and aneural, and its matrix is maintained by chondrocyte-like cells that are stimulated by growth factors to produce components such as elastin, type II collagen, and proteoglycans.[22] It is important to remember that nucleus pulposus cells inhibit the enzymes responsible for matrix breakdown, ensuring a dynamic balance between the degradation and production of these components.[23]

The annulus fibrosus consists of 15 to 25 concentric rings of type I collagen. The cells in the outer annulus fibrosus resemble fibroblasts (elongated and thin, arranged parallel to collagen fibers) while those in the inner annulus tend to be more oval-shaped.[24] Notably, the sensory innervation of a healthy (non-diseased) annulus fibrosus is primarily restricted to its outer lamellae.[25] Posterior annulus and the posterior longitudinal ligament are innervated by Luschka's sinuvertebral nerve, a mixed autonomic and somatic nerve. Meanwhile, the anterior and lateral portions receive innervation from autonomic nerves associated with the paraspinal sympathetic chain, reinforcing the tendency of disc pain to exhibit characteristics like visceral pain.[26]

Finally, it is important to emphasize that both the upper and lower boundaries of the nucleus pulposus and annulus fibrosus are confined by endplates, which are horizontal layers of cartilage approximately 1 mm thick. These endplates are composed of type II collagen, just like the annulus fibrosus, with which they form a strong interwoven structure, unlike their weaker attachment to the vertebral bodies. These endplates are normally avascular and aneural.

The process of intervertebral disc degeneration follows a three-phase cascade proposed by Kirkaldy-Willis and associates. In phase 1 (dysfunction), histological changes include tears or circular fissures in the outer annulus. Since this area is innervated, such damage produces pain. These tears or fissures may also be accompanied by separation or failure of the endplate, leading to reduced nutrient supply to the affected disc and accelerating degeneration. This progresses to phase 2 (instability), characterized by increased pressure in the damaged region, further exacerbating disc degeneration. Finally, in phase 3 (stabilization), biochemical changes result in chronic internal disc disruption (IDD) and disc herniation.[27]

Risk factors for cervical discogenic pain

The reason why some intervertebral discs degenerate prematurely and cause pain while others do not remain a subject of controversy and uncertainty worldwide. However, several factors have been identified that may predispose individuals to developing discogenic pain. Genetics, a history of moderate to severe trauma, intense physical labor, and whole body vibration exposure are among the potential risk factors for developing internal disc disruption (IDD).[28] Additionally, sedentary behavior, obesity, and smoking have been recognized as independent risk factors, separate from disc degeneration.

Heredity is considered the primary risk factor for developing disc degeneration. A family history of spinal surgery triples the likelihood of experiencing cervical and/or lumbar discogenic pain due to a "genetic weakness" in the collagen structure of the disc, its blood supply, or its metabolism. For example, mutations in the COL9A2 and COL9A3 genes, which encode type IX collagen, have been identified as contributors to disc degeneration and sciatica, although they are rare.[28]

The second major risk factor for accelerated disc degeneration and discogenic pain is trauma induced structural damage to either the annulus or the vertebral endplate.[29] Given that the vertebral endplate is the most fracture prone structure within a mobile segment (comprising two vertebrae and the intervertebral disc), it is understandable why accelerated disc degeneration occurs following trauma, even when it is not immediately visible on imaging studies in the early stages.

Regarding occupation, no clear relationship has been identified between employment status and neck pain. However, some occupations are beginning to be recognized as potential risk factors for initiating or exacerbating preexisting neck pain.

Regarding obesity, most evidence suggests no significant relationship between the body mass index and the prevalence of cervical pain.[30]

Smoking significantly reduces cellular absorption and metabolic activity within the disc. Studies have demonstrated

that smoking increases disc degeneration across all intervertebral discs by approximately 20% and is consistently identified as an independent risk factor for cervical pain.[31] [32]

Lastly, psychological pathology is an intriguing and controversial risk factor that has been identified as a potential cause of cervical and lumbar pain. A phase II cohort study identified poor psychological health as an independent risk factor for cervical pain.[33] [34]

Pain Mechanism and Therapeutic Strategies

The pain experienced from an injured intervertebral disc is not solely due to the disc as a primary nociceptive structure. Disc injuries alter the biomechanics of the spinal motion segment (the intervertebral disc and its two adjacent vertebrae), leading to increased loading or traction on the zygapophyseal joints, which are significant contributors to cervical pain.

As a result, therapeutic strategies for discogenic pain focus on three primary objectives:

1) Resolving primary nociception caused by post injury neoinnervation and neovascularization of the posterior annular tear.
2) Restoring or mitigating the pro nociceptive anabolic-catabolic imbalance, including normalizing cytokine immunochemistry within the nucleus-annular biochemical and cellular environment.
3) Restoring mechanical and hydraulic functions, including intervertebral hydrostatic pressure, disc height, and annular integrity.

However, treating only the injured disc is unlikely to fully resolve the pain. The spinal motion segment must be considered as a whole, meaning that the zygapophyseal joints adjacent to the affected disc also contribute to cervical pain in most cases. Therefore, these joints should be included in therapeutic planning to optimize outcomes in alleviating cervical pain following an intervertebral disc injury.

Interventional treatment for cervical pain

We propose a triple minimally invasive interventional approach for managing patients with cervical pain caused by intervertebral disc lesions, considering the spinal motion segment as a dynamic structure with multiple pain generators and exacerbating factors. Under this approach, it is equally important to treat the intervertebral disc, the zygapophyseal (facet) joints at the corresponding level, and the paravertebral musculature of the cervical spine.

The posterior annulus of the lumbar intervertebral disc is normally innervated only in its outermost third, while neoinnervation of the middle or inner thirds, as well as the nucleus pulposus, is limited to pathological pain states. Small annular tears appear to accompany neovascularization and neoinnervation of the normally avascular and non-innervated middle and inner thirds of the annulus. For this reason, thermal intradiscal radiofrequency at the cervical level provides a dual benefit in pathological neoinnervation:

1) Denervation of the painful disc.
2) Retraction effect due to scar formation at temperatures above 65°C for more than 5 minutes.

This mild retraction of the posterior annulus (which may be insignificant in the larger lumbar disc) can provide greater biomechanical relief in the cervical spine, particularly in type I and II disc herniations or disc protrusions, which increase pressure on the posterior longitudinal ligament (a richly innervated structure).

Platelet-Rich Plasma (PRP) Therapy

Platelet-rich plasma (PRP) contains multiple cytokines and has been used to treat a variety of painful musculoskeletal conditions. Intradiscal PRP administration has been proposed as a potentially beneficial treatment for discogenic pain.[35] A randomized clinical trial on intradiscal PRP initiated by Lutz in 2009 for discogenic pain has yet to be fully reported. Therefore, intradiscal PRP administration following intradiscal radiofrequency treatment is proposed as an adjunct therapy in the triple interventional approach for discogenic pain management.

Zygapophyseal Joint Denervation

The zygapophyseal (facet) joint is considered a secondary cause of cervical pain, exacerbating symptoms and contributing to persistent dysfunction of the motion segment (comprising the intervertebral disc, adjacent vertebrae, and facet joints). Facet syndrome should always be addressed when treating a cervical intervertebral disc lesion to ensure comprehensive pain management.

For this reason, we propose thermal radiofrequency denervation of the medial branches at 70°C on two bilateral facet joint levels:

- The level of the cervical herniation.
- One level above the affected disc (due to dual level facet innervation).

This approach ensures effective treatment of articular pain contributions to cervical pain.

Epidural Steroid Injections

Lastly, chronic cervical pain management should include epidural space anti-inflammatory therapy using steroid injections at the nerve root exit zone. This technique delivers adequate concentrations of corticosteroids directly to an inflamed nerve root, minimizing systemic side effects associated with oral or parenteral corticosteroid therapy.

By integrating thermal intradiscal radiofrequency, zygapophyseal joint denervation, and epidural steroid injection, the triple interventional approach provides a comprehensive, minimally invasive treatment for cervical pain, with or without radiculopathy, secondary to Type I and II disc herniations.

Aim of the study

To report the treatment based on the "Triple interventional approach for comprehensive management in cervicalgia, secondary to disc and facet pathology."

2. Methodology

A descriptive case series study was conducted with a follow-up period of six months, covering a span of two years, including 16 patients treated between March 2022 and February 2024. The inclusion criteria were:

- Diagnosis of cervical hernia at a maximum of 1 or 2 levels.
- The cervical pain lasted more than 3 months.
- No history of previous surgery.
- Cervical hernia Grade I and II confirmed by MRI, without extrusion or sequestration.
- Refractoriness in pharmacological management and physical therapy.
- Minimum score of 5/10 on Numeric Rating Scale (NRS) for pain.

The patients underwent the triple interventional approach protocol described below:

Cervical Intradiscal Radiofrequency
A 100mm-20G-10mm cannula with a curved tip was used for fluoroscopy guided navigation in anteroposterior and lateral views. A right paratracheal approach was performed, inserting the cannula anteriorly and directing it towards the posterior annulus, with slight rotation towards the side of hernia lateralization and the presence of radiculopathy.

Motor neurostimulation tests were performed to ensure no response at 1.2 V. If a motor response was obtained at a lower voltage, the cannula was repositioned to prevent nerve damage.

Subsequently, intra discal therapy was performed with the following parameters:
1) Time: 440 seconds
2) Temperature:
   - 55°C (0-60s)
   - 60°C (61-120s)
   - 65°C (121-420s)
   - 70°C (421-440s)

After completing the therapy, the active tip temperature was allowed to drop to 42°C before removing the electrode. 0.5 ml of PRP was injected into the posterior and 0.5 ml into the anterior annulus using a sterile technique, concluding the first approach of the protocol.

Radiofrequency of medial branches for facet joint arthropathy treatment
With the patient in prone position, asepsis and antisepsis of the posterior cervical and thoracic area were performed. Fluoroscopy was used to guide the placement of 100mm-20G-5mm cannulas with curved tips in the medial branches of the facet levels of the cervical hernia and one superior level.

Neurostimulation tests were performed with a motor response expected between 0.3 and 0.5 mV. Subsequently, 0.3 ml of 1% lidocaine was administered, and thermal radiofrequency was applied with the following parameters:
- Time: 440 seconds
- Temperature: 65°C

Upon completion, the temperature was allowed to drop to 42°C before removing the cannula, followed by the administration of 0.5 ml of 0.25% bupivacaine. This approach ensured comprehensive treatment of the associated facet syndrome.

Cervical epidural steroid injection
An interlaminar approach was performed at the C7-T1 or C6-C7 level using a Touhy #18 needle, applying the loss-of-resistance technique with air. The correct drug distribution in the epidural space was confirmed with an epidurography using 3 ml of contrast solution.

The following were then administered:
- Dexamethasone 16 mg (4 ml volume).
- Total volume of 10 ml (including 7 ml of steroid and saline solution mix, plus 3 ml of the contrast solution for epidurography).

The Touhy needle was withdrawn after administering 1 ml of 1% lidocaine, thus concluding the "Triple interventional approach for comprehensive management in cervicalgia, secondary to grade I and II hernias" protocol.

3. Results

A total of 19 procedures were performed on 16 patients, as 3 patients had 2 cervical hernias with the previously described characteristics. The total number of patients was 16, with a distribution of 11 female and 5 male patients, ages ranging from 27 to 80 years, with a mean age of 51.5 years, weights ranging from 50 to 117 kg with a mean weight of 72.3 kg, and an average height of 166 cm (150-182 cm). Three patients had type 2 diabetes mellitus (DM2) as a comorbidity, all with good glycemic control and hemoglobin A1c levels below 6.5%, and 5 patients had systemic arterial hypertension under adequate control. The 3 patients with diabetes mellitus are part of the 5 patients with hypertension.

Of the 16 patients, 13 had cervical radiculopathy with different distributions, and only 3 patients had solely mechanical cervical pain. All patients had a minimum NRS score of 5 or higher, and all have had cervical pain for more than 3 months, having received pharmacological treatments and at least 1 month of physical rehabilitation before considering the interventional procedure. Nine patients had a hernia at the C5-C6 level, 5 patients had a hernia at the C6-C7 level, 4 patients had a hernia at the C4-C5 level, and only 1 patient had a hernia at the C3-C4 level. The 3 patients who had two hernias were among the previously mentioned ones. It was found that 2 of these 3 patients had hernias at C4-C5 and C5-C6, and 1 patient had hernias at C5-C6 and C6-C7. These 3 patients underwent the approach at both levels of their corresponding cervical hernias, and radiofrequency was performed at an additional zygapophysial level.

All patients had a minimum NRS score of 5 out of 10, with a maximum of 9 points for 2 patients and a minimum of 5 points for 5 patients. The mean NRS score prior to the procedure was 6.5. Follow-up was conducted at 1, 3, and 6 months for all patients. The mean NRS score at 6 months was 1.9, with 1 patient returning to their initial NRS score of 5 at 6 months, and 2 patients reporting an NRS score of 4 at 6 months of follow-up, with all 3 patients experiencing moderate intensity pain. These patients were considered to have an unsuccessful treatment outcome, which corresponds to 18.7% of the treated population.

4. Discussion

We consider the "Triple interventional approach for comprehensive management in cervicalgia, secondary to disc and facet pathology" as an option for managing cervical pathology secondary to grade I and II hernias, with results that require more studies to consider the treatment as a viable option for patients with chronic pain, positioned between conservative pharmacological treatments and surgical options. In our case series with the established protocol, the results appear to be positive; however, we believe that the variations in the population necessitate a larger sample size.

All patients, after the triple approach, continued with 10 sessions of physical therapy over 30 days with the aim of improving and restoring the best functionality of the cervical spine. This allowed for a therapeutic window free of pain secondary to the interventional management. We consider physical therapy to be a fundamental pillar for long-term management in all patients with any level of spinal pathology, and it should always be included in both conservative treatments and interventional and surgical approaches, as we regard patients with spinal pathology (cervical, thoracic, and lumbar) as individuals with chronic conditions.

5. Conclusions

The "Triple interventional approach for comprehensive management in cervicalgia, secondary to grade I and II hernias" represents a management strategy aimed at addressing the 3 main sources of pain when intervertebral disc pathology exists in grade I and II hernias, considering the intervertebral disc, facet joints, and related nerve roots as the primary sources of cervical pain. By considering the mobile unit of the spine as a functional complex of anatomically related structures (intervertebral disc, adjacent vertebrae, facet joints, and nerve roots), it is important to recognize that any chronic pain should consider the involvement of any of these 3 structures and treat them accordingly.

Acknowledgement
The authors thank everyone who supported this effort.

Conflict of interest
The authors declare no potential conflict of interests.

Author contributions
All authors contirbuted equally to the data research, discussion, writing, and revising of the manuscript.

References

[1] Mooney V: Where is the pain coming from? Spine 12:754-759, 1987.
[2] Rhyne AL et al: Outcome of unoperated discogram-positive low back pain. Spine 20:1997-2000, 1995.
[3] Inman VT, Saunders JB: Anatomical and physiological aspects of injuries to the intervertebral disc. J Bone Joint Surg 29:461, 1947.
[4] Crock HV: A reappraisal of intervertebral disc lesions. Med J 1:983-989, 1970.
[5] The American Heritage dictionary of the English language, ed 4, Boston, 2000, Houghton Mifflin, updated 2009.
[6] Bogduk N, Windsor M, Inglis A: The innervation of the cervical intervertebral discs. Spine 13:2-8, 1988.
[7] Wilberg G: Back pain in relation to the nerve supply of the intervertebral disc. Acta Orthop Scand 19:211-212, 1949.
[8] Edgar MA Nundy S: Innervation of the spinal dura mater. J Neurol Neurosurg Psychiatry 29:530-534, 1966.
[9] Bogduk N, Windsor M Inglis A: The innervations of the cervical intervertebral discs. Spine 13(1):2-8, 1988.
[10] Martin BI et al: Expenditures and health status among adults with back and neck problems. JAMA 299(6)656-664, 2008.
[11] Bogduk N, Aprill C: On the nature of neck pain, discography and cervical zygapophysial joint blocks. Pain 54(2):213-217, 1993.
[12] Yin W, Bogduk N: The nature of neck pain in a private pain clinic in the United States. Pain Med 9:196-203, 2008.
[13] Weishaupt D et al: MR imaging of the lumbar spine: prevalence of intervertebral disk extrusion and sequestration, nerve root compression, end plate abnormalities, and osteoarthritis of the facet joints in asymptomatic volunteers. Radiology 209:661-666, 1998.
[14] Freemont AJ et al: Nerve ingrowth into diseased intervertebral disc in chronic back pain. Lancet 350(9072):178-181, 1997.
[15] Brisby H: Pathology and possible mechanisms of nervous system response to disc degeneration. J Bone Joint Surg (Am) 88(suppl 2):68-71, 2006.
[16] Roberts S et al: Mechanoreceptors in intervertebral discs: morphology, distribution and neuropeptides. Spine 20:2645-2651, 1995.
[17] Morinaga T et al: Sensory innervations to the anterior portion of lumbar intervertebral disc. Spine 21:1848-1851, 1996.
[18] Brown MF et al: Sensory and sympathetic innervations of the vertebral endplate in patients with degenerative disc disease. J Bone Joint Surg (Br) 79-B:147-153, 1997.
[19] Mooney V: Where is the pain coming from? Spine 12:754-759, 1987.
[20] Twomey LT, Taylor JR: Age changes in lumbar vertebrae and intervertebral discs. Clin Orthop 224:97-104, 1987.
[21] Yoshizawa H, O'Brien JP, Smith WT, Trumper M: The neuropathy of intervertebral disc removed for low back pain. Lancet 350:178-181, 1997.
[22] Freemont AJ: The cellular pathobiology of the degenerate intervertebral disc and discogenic back pain. Rheumatology (Oxford) 48(1):5-10, 2009.
[23] Matrisian LM: Metalloproteinases and their inhibitors in matrix remodeling. Trends Genet 6:121-125, 1990.
[24] Marchand F, Ahmed AM: Investigation of the laminate structure of lumbar disc anulus fibrosus. Spine 15:402-410, 1990.
[25] Roberts S et al: Mechanoreceptors in intervertebral discs: morphology, distribution, and neuropeptides. Spine 20:2645-2651, 1995.

[26] Bogduk N: The innervation of the intervertebral discs. In Boyling JD, Palastanga N, editors: Grieve's modern manual therapy-the vertebral column, Edinburgh, UK 1994, Churchill Livingstone.
[27] Kirkaldy- Willis W et al: Pathology and pathogenesis of lumbar spondylosis and stenosis. Spine 3(4) 318-328, 1978.
[28] Cassinelli EH, Hall RA, Kang JD: Biochemistry of intervertebral disc degeneration and the potential for gene therapy applications. Spine J I(3):205-214, 2001.
[29] Adams MA et al: Mechanical initiation of intervertebral disc degeneration. Spine 25(13):1625-1636, 2000.
[30] Webb R et al: Prevalence and predictors of intense, chronic, and disabling neck and back pain in the UK general population. Spine 28:1195-1202, 2003.
[31] Croft PR et al: Risk factors for neck pain: a longitudinal study in the general population. Pain 93:317-325, 2001.
[32] Kelsey JL et al: An epidemiological study of acute prolapsed cervical intervertebral disc. J Bone Joint Surg (AM) 66:907-914, 1984.
[33] Croft PR et al: Risk factors for neck pain: a longitudinal study in the general population. Pain 93:317-325, 2001.
[34] Siivola SM et al: Predictive factors for neck and shoulder pain: a longitudinal study in young adults. Spine 19:1662-1669, 2004.
[35] Chen WH, et al: Intervertebral disc regeneration in an ex vivo culture system using mesenchymal stem cells and platelet-rich plasma. Biomaterials 30(29):5523-5533, 2009.

Annexes

Table 1

Patient	Age	Sex	Occupation	Weight (kg)	Height (m)
1	44	M	Construction	72	1.67
2	43	M	Technician	117	1.82
3	60	F	Homemaker	47	1.6
4	61	F	Homemaker	68	1.68
5	80	F	Homemaker	75	1.62
6	41	M	Teacher	100	1.78
7	48	F	Homemaker	64	1.55
8	57	F	Homemaker	57	1.58
9	39	F	Homemaker	70	1.63
10	54	F	Homemaker	53	1.5
11	53	M	Federal Employee	98	1.75
12	65	F	Homemaker	67	1.7
13	66	M	Engineer	86	1.82
14	24	F	Dentist	50	1.65
15	62	F	Stylist	71	1.67
16	27	F	Veterinarian	63	1.62

Table 2

Patient	DM	HT	Radiculopathy	Diagnosis	Initial NRS	NRS 1 M	NRS 3 M	NRS 6 M
1	No	No	Yes	Cervical Hernia C5-C6	5	0	0	1
2	No	No	Yes	Cervical Hernia C5-C6	6	0	2	2
3	No	No	No	Cervical Hernia C5-C6	6	2	2	1
4	No	Yes	Yes	Cervical Hernia C4-C5	5	1	0	5
5	No	Yes	Yes	Cervical Hernia C4-C5 and C5-C6	7	2	2	2
6	No	No	Yes	Cervical Hernia C6-C7	5	1	3	2
7	Yes	Yes	Yes	Cervical Hernia C5-C6 and C6-C7	8	0	0	1
8	No	No	Yes	Cervical Hernia C4-C5 and C5-C6	6	2	1	1
9	No	No	Yes	Cervical Hernia C6-C7	9	2	1	2
10	No	No	No	Cervical Hernia C5-C6	6	2	2	1
11	No	No	Yes	Cervical Hernia C5-C6	5	0	1	0
12	Yes	Yes	Yes	Cervical Hernia C4-C5	8	0	1	3
13	No	No	Yes	Cervical Hernia C3-C4	7	2	2	4
14	No	No	Yes	Cervical Hernia C6-C7	9	1	2	4
15	Yes	Yes	Yes	Cervical Hernia C6-C7	5	0	0	0
16	No	No	No	Cervical Hernia C5-C6	7	0	0	3

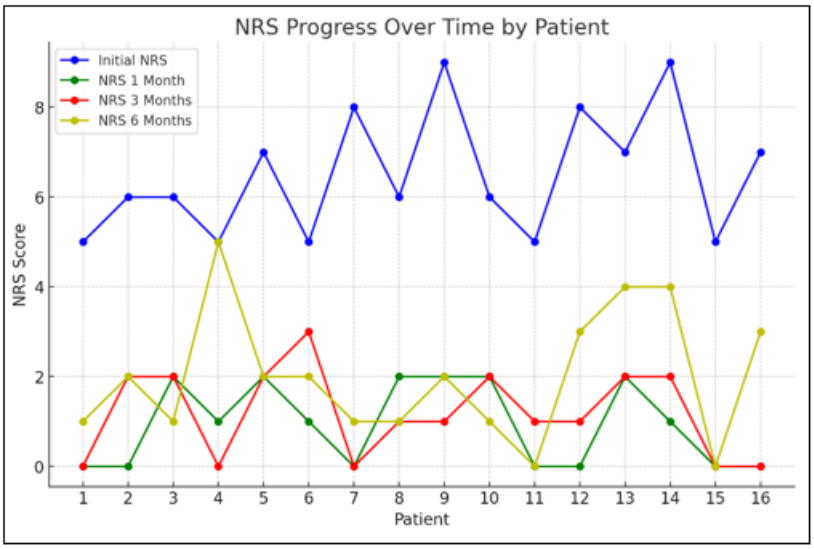
NRS Progress Over Time by Patient
Initial NRS
NRS 1 Month
NRS 3 Months
NRS 6 Months
NRS Score
Patient
0
2
4
6
8
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Figure 1