Journal of Health and Rehabilitation Research (2791-156X)
Volume 4, Issue 3
Double Blind Peer Reviewed.
https://jhrlmc.com/
DOI: https://doi.org/10.61919/jhrr.v4i3.1519
www.lmi.education/

Comparison of Effects of Transcutaneous Electrical Nerve Stimulation and Core Stability Exercises on Pain and Disability in Disc Herniation: A Randomized Clinical Trial

Sania Naz[1], Nida Ilahi[2], Muhammad Shaheer Younis[3], Ahmad Ghulam Mahyuddin[4], Saba Fatima[4], Kiran Mehmood[5], Zarafshan[6], Muqadas Rafiq[6]

Correspondence
Sania Naz
saaniaanaz@gmail.com

Affiliations
1 Lecturer, Government College University Faisalabad, Layyah Campus, Pakistan
2 Head of Department, Government College University Faisalabad, Layyah Campus, Pakistan
3 The Irus Polyclinic & Rehabilitation Center, Multan, Pakistan
4 Allied Hospital, Faisalabad, Pakistan
5 DHQ, Bhakkar, Pakistan
6 DHQ, Kot Addu, Pakistan

Keywords
Lumbar disc herniation, Transcutaneous Electrical Nerve Stimulation, Core Stability Exercises, chronic low back pain, pain management, disability reduction, randomized clinical trial, non-invasive treatment.

Disclaimers

Authors' Contributions	All authors contributed equally to the work of this study.
Conflict of Interest	None declared
Data/supplements	Available on request.
Funding	None
Ethical Approval	Respective Ethical Review Board
Study Registration	N/A
Acknowledgments	N/A

ABSTRACT

Background: Lumbar disc herniation is a common cause of chronic low back pain, often leading to significant pain and disability. Non-invasive interventions such as Transcutaneous Electrical Nerve Stimulation (TENS) and Core Stability Exercises (CSE) are frequently used for symptom management, but their comparative effectiveness remains unclear.

Objective: To compare the effects of TENS and CSE on pain intensity and disability in patients with lumbar disc herniation.

Methods: This randomized clinical trial included 10 subjects aged 18-60 years, divided into two groups: Group A (TENS) and Group B (CSE). Both groups received their respective interventions over eight weeks, with pain and disability assessed using the Numeric Pain Rating Scale (NPRS) and the Modified Oswestry Disability Index (MODI). Data were analyzed using SPSS version 27.0, with a significance level set at $p<0.05$.

Results: Group A showed a reduction in NPRS from 3.80 ± 0.83 to 2.40 ± 0.54 ($p=0.005$) and in MODI from 4.80 ± 0.44 to 3.60 ± 0.89 ($p=0.033$). Group B demonstrated a reduction in NPRS from 3.60 ± 1.14 to 1.40 ± 0.54 ($p=0.020$) and in MODI from 3.20 ± 0.44 to 1.20 ± 0.44 ($p=0.003$).

Conclusion: Both TENS and CSE effectively reduced pain and disability in lumbar disc herniation patients, with CSE showing superior results.

INTRODUCTION

Disc herniation is a common musculoskeletal disorder characterized by the protrusion or extrusion of the soft, gel-like centre of a spinal disc from its normal position, often resulting in significant lower back pain that radiates down to the legs. This condition is widely recognized as a major cause of sciatica and affects a substantial portion of individuals with chronic lower back pain, with estimates suggesting that approximately 39% of those affected experience symptoms linked to disc herniation (1). The pain typically follows the path of the sciatic or femoral nerve and can significantly impact a person's daily functioning and quality of life. Epidemiological studies have shown that low back pain is prevalent, with around 90% of people experiencing it at least once in their lives, and about 10% of individuals developing disc herniation at some point (2). Interestingly, anatomical studies indicate that 20-40% of people have asymptomatic disc herniation detectable only through imaging, and although only 2-5% of patients presenting with back pain are diagnosed with disc herniation, a significant 40% of those seeking medical help for low back pain are found to have this condition (2). Lumbar disc herniation (LDH) specifically refers to the bulging of a spinal disc in the lower back, often due to factors such as wear and tear, aging, or external mechanical stress (3).

The muscles that play a crucial role in maintaining trunk stability and supporting the spine include the multifidus, erector spinae, rectus abdominis, internal and external obliques, and the transverse abdominis (4). These muscles work in concert to stabilize the trunk, reduce the risk of further injury, and mitigate strain on the spinal structures. LDH is often associated with degenerative changes in the spine, leading to a spectrum of symptoms such as stiffness, nerve root pain, and disc prolapse, all of which can impose a considerable burden on healthcare resources and significantly affect individuals' health and quality of life (5). The progression of LDH involves a series of changes within the disc structure, culminating in the prolapse of the disc, which can present with symptoms including lower back pain, numbness, tingling sensations, muscle stiffness, weakness in the lower extremities, and nerve compression (6). The variability in symptom severity is influenced by both the degree of herniation and individual differences in nervous system sensitivity, with some individuals experiencing debilitating pain and restricted mobility (7).

Transcutaneous Electrical Nerve Stimulation (TENS) is a widely used electrotherapeutic intervention aimed at providing pain relief by delivering mild electrical currents through the skin to stimulate sensory nerves (8). The primary mechanism involves the activation of low-threshold nerves that inhibit nociceptive signals, thereby blocking pain transmission along afferent pathways, reducing

sympathetic activity, and promoting the release of endogenous opioids. TENS is underpinned by various theoretical frameworks, including the widely accepted gate control theory, which posits that the stimulation of non-painful input can inhibit the perception of pain (9). Although TENS has been shown to provide immediate pain relief in some individuals, its efficacy as a standalone treatment for preventing fatigue and reducing functional disability in disc herniation patients remains a subject of ongoing research (9). Different forms of TENS, including conventional, acupuncture-like, and variable frequency-intensity modalities, are employed based on clinical judgment and patient needs, each aiming to optimize pain management through peripheral nerve stimulation (10).

Core stability exercises, another non-invasive therapeutic approach, target the core muscles, including the abdominals and back muscles, to enhance strength, stability, and neuromuscular control. These exercises aim to restore the functionality of the muscles that stabilize the trunk and improve dynamic spinal stability, thereby mitigating pain and disability in patients with LDH (11). The effectiveness of core stability exercises is often evaluated using tools such as the Modified Oswestry Low Back Pain Disability Questionnaire (MOLBPDQ), which measures the extent of disability across various domains of daily living activities, providing a quantifiable outcome of therapeutic interventions (12). Core stability exercises have been reported to reduce pain, enhance range of motion, and improve the endurance and strength of muscles essential for maintaining spinal stability (13). The exercises typically include a range of movements such as bridging, planks, and other functional exercises that engage both superficial and deep muscle groups to support the spine and alleviate symptoms associated with LDH (14).

The current study builds on previous research exploring the effects of TENS and core stability exercises in managing pain and disability among patients with disc herniation. Evidence from Romas et al. (2018) suggests that while TENS is effective for immediate pain relief, core stability exercises are superior in improving fatigue and functional outcomes in LDH patients (1). Similarly, studies by Jeongil Kang et al. (2019) and Fabio Jorge Renovato Franca et al. (2019) have demonstrated the potential of core stability exercises in enhancing neuromuscular control and reducing motor neuron excitability, highlighting their broader therapeutic benefits beyond pain relief alone (3, 9). Comparative analyses have also shown that core stability exercises can effectively coordinate pain and improve muscle activation in patients with disc herniation, underscoring the importance of a multifaceted approach that combines TENS for acute symptom relief with core stability exercises for long-term functional improvements (13). The objective of this study is to compare the effects of TENS and core stability exercises on pain and disability in patients with disc herniation, with the aim of identifying a comprehensive therapeutic strategy that addresses both immediate and sustained pain relief while enhancing muscle function and endurance. This investigation will provide valuable insights into optimizing non-invasive interventions for managing disc herniation, ultimately contributing to improved patient outcomes in clinical practice.

MATERIAL AND METHODS

The study was designed as a randomized clinical trial and was conducted at Layyah City Hospital over a period of six months following the approval of the research topic. The sample size was calculated using pre-treatment values of functional disability measured by the Oswestry Disability Index (ODI) with the Epitool calculator, which resulted in a required sample size of 10 participants, with 5 individuals in each group. Participants were divided into two study groups: Group A, which received Transcutaneous Electrical Nerve Stimulation (TENS), and Group B, which participated in Core Stability Exercises (CSE). A non-probability purposive sampling technique was used to recruit participants, with inclusion criteria including patients referred by neurophysicians, aged between 18 to 60 years, experiencing pain for more than three months, and both male and female participants (1, 9, 15). Exclusion criteria encompassed patients with a history of lumbar surgery, carcinoma, involvement in sports or load training for the spine for more than three months prior to treatment, rheumatologic diseases, other causes of back pain such as lumbar spinal stenosis, and spondylolisthesis (1, 15).

Data collection was performed using the Numeric Pain Rating Scale (NPRS) and the Modified Oswestry Disability Index (MODI). The NPRS is a validated and reliable tool for measuring pain intensity on a scale from 0 (no pain) to 10 (most severe pain), frequently used in various acute pathologies (16). The MODI is a standardized questionnaire consisting of 10 items that assess functional disability in daily activities, including pain intensity, personal care, lifting, working, sitting, standing, sleeping, employment, homemaking, social life, and traveling. Each item is rated from 0 to 5, with a maximum score of 50, providing a measure of the impact of lumbar disc herniation on functional abilities (17).

The study protocol was approved by the ethical committee of GCUF Layyah Campus, and all procedures were conducted in accordance with the Declaration of Helsinki. Participants provided written informed consent prior to enrollment. Eligible participants, as confirmed by neurophysician referrals and MRI findings indicating disc herniation, were randomized into two equal groups using the lottery method. The study employed a single-blind design, ensuring that participants were unaware of their group assignments. Group A participants received TENS therapy, which included a heating pad as a baseline treatment for 10 to 15 minutes to alleviate muscle tension, followed by TENS administered for 60 minutes with pulses of 50 to 80 ms duration and a frequency of 20 Hz. Electrodes were placed bilaterally on the lumbar paraspinal points to target the affected areas (1, 18). Group B participants received the same baseline heating pad treatment, followed by Core Stability Exercises (CSE) administered three days per week over eight weeks, totaling 24 sessions. Each session lasted for 60 minutes and included exercises progressing from 1 to 3 sets, 8 to 15 repetitions, and contractions from 5 to 10

seconds, with rest intervals set at 30 seconds between sets and 2 to 3 minutes between exercises. The exercises included abdominal pull-ins in a supine position, abdominal pulls with knee flexion towards the chest, heel slides, prone cobra, supine superman, and planks, all designed to enhance core muscle activation and spinal stability (2, 19).

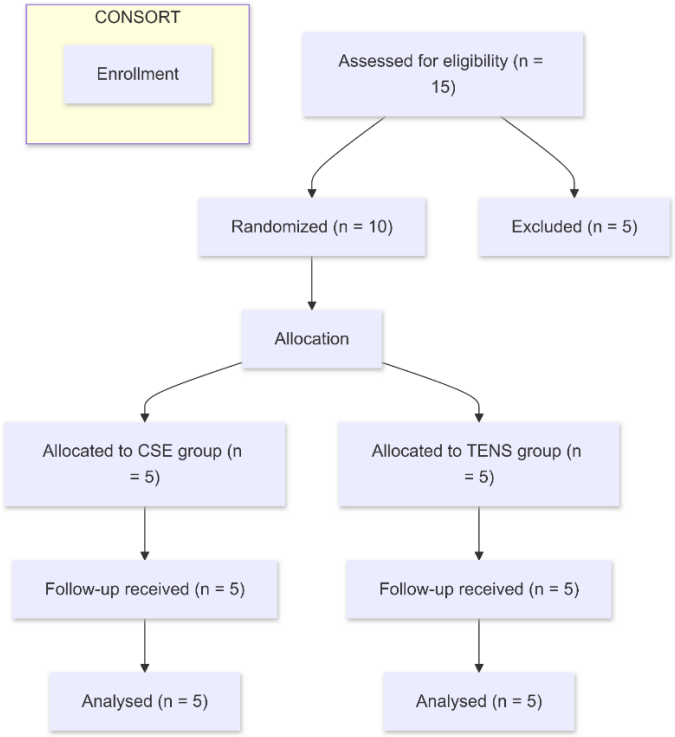

Figure 1 CONSORT Flowchart

Data were managed and analyzed using SPSS version 27.0. Descriptive statistics were used to summarize the quantitative data as mean ± standard deviation (SD). An independent t-test was employed to compare clinical outcomes between the two groups both before and after the intervention. A p-value of less than 0.05 was considered statistically significant, indicating a meaningful difference between the treatment effects of TENS and CSE on pain and disability in patients with disc herniation. The results of the study aimed to provide evidence on the effectiveness of these non-invasive interventions in managing symptoms associated with lumbar disc herniation, ultimately contributing to the body of knowledge on conservative management strategies for this condition.

RESULTS

The study compared the effects of Transcutaneous Electrical Nerve Stimulation (TENS) and Core Stability Exercises (CSE) on various clinical outcomes in patients with lumbar disc herniation. Below are the results presented in tabular format and described in paragraphs for clarity.

The demographic and clinical characteristics of participants in both groups were comparable at baseline. There were no significant differences in age, gender distribution, or initial measures of pain intensity (NPRS) and functional disability (MODI) between the two groups, as indicated by p-values greater than 0.05.

Both Group A (TENS) and Group B (CSE) showed significant improvements in various clinical outcomes following the intervention. For pain intensity, Group B (CSE) demonstrated a greater mean reduction (2.20 ± 1.30) compared to Group A (TENS) (1.40 ± 0.54), with both groups achieving statistically significant improvements (p = 0.020 for Group B, p = 0.005 for Group A).

Table 1: Baseline Demographic and Clinical Characteristics

Characteristic	Group A (TENS)	Group B (CSE)	p-value
Age	31.80 ± 10.05	39.20 ± 11.14	> 0.05
Gender	1.57 ± 0.53	1.43 ± 0.53	> 0.05
NPRS	1.20 ± 0.44	2.20 ± 0.83	> 0.05
MODI	1.20 ± 0.83	2.00 ± 0.70	> 0.05

CSE: TENS, Transcutaneous Electrical Stimulation, Core Stability Exercises

Table 2: Clinical Outcomes Pre and Post Intervention

Measure	Group A, Pre, Post-Treatment M± S.D., MC,				Group B, Pre, Post-Treatment M± S.D., MC,			
	Pre-	Post-	MC ± S.D.	p-value	Pre-	Post-	MC ± S.D.	p-value
Pain Intensity	3.80 ± 0.83	2.40 ± 0.54	1.40 ± 0.54	0.005	3.60 ± 1.14	1.40 ± 0.54	2.20 ± 1.30	0.020
Personal Care	4.00 ± 0.70	2.60 ± 0.54	1.40 ± 0.89	0.025	3.40 ± 1.14	1.60 ± 0.54	1.80 ± 0.83	0.009
Lifting	4.00 ± 0.70	2.20 ± 0.44	1.80 ± 0.83	0.009	3.80 ± 1.30	1.60 ± 0.54	2.20 ± 0.83	0.004
Walking	3.80 ± 0.83	3.00 ± 0.00	0.80 ± 0.83	0.099	3.60 ± 1.14	1.80 ± 0.44	1.80 ± 0.83	0.009
Sitting	4.20 ± 0.83	2.60 ± 0.54	1.60 ± 0.54	0.003	3.20 ± 0.83	1.60 ± 0.54	1.60 ± 0.54	0.003
Standing	4.00 ± 0.70	2.60 ± 0.54	1.40 ± 1.14	0.052	3.40 ± 1.14	1.60 ± 0.54	1.80 ± 1.09	0.021
Sleeping	4.00 ± 0.70	2.60 ± 0.54	1.40 ± 0.89	0.025	3.20 ± 0.83	1.60 ± 0.54	1.60 ± 0.54	0.003
Social Life	4.00 ± 0.70	2.80 ± 0.44	1.20 ± 0.83	0.033	3.40 ± 1.14	1.60 ± 0.54	1.80 ± 1.48	0.053
Travelling	3.80 ± 0.83	2.80 ± 0.44	1.00 ± 1.22	0.242	3.60 ± 1.14	1.60 ± 0.54	2.00 ± 1.00	0.021
Employment/ADL	4.20 ± 0.83	2.60 ± 0.54	1.60 ± 0.54	0.003	3.20 ± 0.83	1.60 ± 0.54	1.60 ± 1.14	0.035

M: Mean, S.D. Standard Deviation, MC: Mean Change

In personal care tasks, both groups improved significantly; however, the improvement was more pronounced in Group B (CSE) with a mean change of 1.80 ± 0.83 (p = 0.009) compared to Group A's mean change of 1.40 ± 0.89 (p =

0.025). Similar trends were observed for lifting and walking, where the CSE group consistently outperformed the TENS group in terms of mean change and statistical significance.

For measures like sitting, both groups showed identical improvements (mean change of 1.60 ± 0.54) with the same level of significance (p = 0.003). In terms of standing, sleeping, social life, and traveling, Group B (CSE) consistently showed either significant improvements or improvements that were trending toward significance compared to Group A (TENS). Specifically, the CSE group's performance in enhancing traveling capabilities was notably higher (mean change of 2.00 ± 1.00, p = 0.021) compared to the TENS group (mean change of 1.00 ± 1.22, p = 0.242).

Overall, the results indicate that Core Stability Exercises (CSE) were generally more effective than Transcutaneous Electrical Nerve Stimulation (TENS) in reducing pain and improving functional outcomes across various domains in patients with lumbar disc herniation. Both interventions contributed to significant improvements; however, the magnitude of these changes was typically greater in the CSE group.

DISCUSSION

This study evaluated the effects of Transcutaneous Electrical Nerve Stimulation (TENS) and Core Stability Exercises (CSE) on pain and disability in patients with lumbar disc herniation. Ten subjects, aged between 18 and 60 years, were divided into two groups: Group A received TENS, and Group B performed CSE. Both interventions were assessed at baseline and after eight weeks of treatment. The findings demonstrated significant reductions in pain intensity and disability scores in both groups; however, the CSE group exhibited a more pronounced improvement, suggesting that core stability exercises may be more effective in managing symptoms of disc herniation. These results align with previous studies that have explored similar interventions in disc herniation patients.

Romas et al. (2018) compared TENS with stabilization exercises, reporting that stabilization exercises significantly improved pain, fatigue, and functional disability in patients with lumbar disc herniation, whereas TENS was only effective for pain relief (1). The current study corroborates these findings, showing that while both interventions reduced pain, CSE had a broader impact on disability, as reflected by lower Modified Oswestry Disability Index (MODI) scores in the CSE group (p = 0.003) compared to the TENS group (p = 0.033). Similarly, Jeongil Kang et al. (2019) found that lumbar stabilization exercises lowered motor neuron excitability and improved neurological symptoms in disc herniation patients, further supporting the use of core stability interventions in this population (3). In this study, reductions in pain were significant in both groups, but the greater improvement in disability observed in the CSE group suggests enhanced neuromuscular control and spinal support mechanisms.

Fabio Jorge Renovato Franca et al. (2019) reported that motor control training was more effective than TENS in reducing pain and functional disability, with improvements in muscle activation (9). The present findings are consistent with this, as CSE, which targets core muscle activation, demonstrated greater efficacy in reducing disability compared to TENS. Furthermore, Yasser Mohebbi Rad et al. (2021) compared suspension exercises and core stability exercises, highlighting the superior effects of suspension exercises on muscle activation and pain reduction (13). The current study's results suggest that CSE alone, even without suspension techniques, provides significant benefits in managing disc herniation, as evidenced by improvements in MODI scores. Mohammad Abbas Jamil et al. (2023) also emphasized the effectiveness of CSE in enhancing back muscle endurance and reducing low back pain and disability after an eight-week intervention, findings that resonate with the current study's outcomes, particularly in the significant improvements observed in pain and functional capacity in the CSE group (2).

This study's strengths include its randomized design and the use of validated outcome measures such as the Numeric Pain Rating Scale (NPRS) and MODI. However, the study's limitations must be acknowledged. The small sample size limits the generalizability of the findings, and the short intervention period without long-term follow-up restricts the ability to assess the sustainability of the observed benefits. Furthermore, the lack of a control group prevents a clearer delineation of the effects attributable solely to the interventions compared to no treatment. Future research should consider larger sample sizes and longer follow-up periods to better understand the durability of the interventions' effects. Additionally, exploring the combination of core stability exercises with other therapeutic modalities may yield further insights into optimal management strategies for disc herniation.

CONCLUSION

Both TENS and core stability exercises were effective in reducing pain and disability in patients with lumbar disc herniation, with core stability exercises showing a statistically significant greater impact on pain intensity and functional improvement. These findings suggest that incorporating core stability exercises into rehabilitation programs could enhance patient outcomes, providing a non-invasive approach to managing disc herniation and potentially improving quality of life and functional independence for affected individuals. Future studies should continue to refine and validate these interventions, aiming to optimize therapeutic strategies for patients with lumbar disc conditions.

REFERENCES

1. Ramos LAV, Callegari B, França FJR, Magalhães MO, Burke TN, Carvalho APdMC, et al. Comparison Between Transcutaneous Electrical Nerve Stimulation and Stabilization Exercises in Fatigue and Transversus Abdominis Activation in Patients With Lumbar Disk Herniation: A Randomized Study. Journal of Manipulative and Physiological Therapeutics. 2018;41(4):323-31.
2. Jamil MA, Bashir MS, Noor R, Niazi R, Ahmad N, Ahmad S, et al. Effects of Core Stabilization Exercises on Low

Back Pain, Disability and Back Muscle Endurance in Patients With Lumbar Disc Herniation. Annals of King Edward Medical University. 2023;29(2):123-8.
3. Kang J, Jeong D, Choi H. Effects of Lumbar Stabilization Exercise on Motor Neuron Excitability and Pain in Patients With Lumbar Disc Herniation. Journal of International Academy of Physical Therapy Research. 2019;10(2):1785-90.
4. Gulsen M, Koz M. Effect of Proprioceptive Neuromuscular Facilitation and Lumbar Stabilization Exercises on Muscle Strength and Muscle Endurance in Patients With Lumbar Disc Hernia. European Journal of Physical Education and Sport Science. 2019.
5. Zhang X, Bi X, Shao J, Sun D, Zhang C, Liu Z. Curative Effects on Muscle Function and Proprioception in Patients With Chronic Lumbar Disk Herniation Using Isokinetic Trunk Muscle Strength Training. Int J Clin Exp Med. 2019;12(4):4311-20.
6. Sharma J, Kumar N, Kumar S. Comparison of the Effectiveness of Core Strengthening Exercise and McKenzie Extension Exercise on the Pain Functional Disability in Lumbar PIVD Condition.
7. Zhou Z. Progress of Core Strength Training Intervention for Lumbar Disc Herniation. Highlights in Science, Engineering and Technology. 2023;54:94-9.
8. Yilmaz M, Tarakci D, Tarakci E. Comparison of High-Intensity Laser Therapy and Combination of Ultrasound Treatment and Transcutaneous Nerve Stimulation on Cervical Pain Associated With Cervical Disc Herniation: A Randomized Trial. Complementary Therapies in Medicine. 2020;49:102295.
9. França FJR, Callegari B, Ramos LAV, Burke TN, Magalhães MO, Comachio J, et al. Motor Control Training Compared With Transcutaneous Electrical Nerve Stimulation in Patients With Disc Herniation With Associated Radiculopathy: A Randomized Controlled Trial. American Journal of Physical Medicine & Rehabilitation. 2019;98(3):207-14.
10. Paley CA, Wittkopf PG, Jones G, Johnson MI. Does TENS Reduce the Intensity of Acute and Chronic Pain? A Comprehensive Appraisal of the Characteristics and Outcomes of 169 Reviews and 49 Meta-Analyses. Medicina. 2021;57(10):1060.
11. Pratama AD, Salam ME. The Effectiveness of Core Stability Exercise to Improve Functional Ability in a Lumbar Herniated Nucleus Pulposus Patient: A Case Study. Physical Therapy Journal of Indonesia. 2021;2(2):61-6.
12. Nwodo OD, Ibikunle PO, Ogbonna NL, Ani KU, Okonkwo AC, Eze CJ, et al. Review of Core Stability Exercise Versus Conventional Exercise in the Management of Chronic Low Back Pain. African Health Sciences. 2022;22(4):148-67.
13. Mohebbi Rad Y, Fadaei Chafy MR, Elmieh A. Is the Novel Suspension Exercises Superior to Core Stability Exercises on Some EMG Coordinates, Pain and Range of Motion of Patients With Disk Herniation? Sport Sciences for Health. 2021:1-11.
14. Ariel E, Levkovitz Y, Goor-Aryeh I, Motti R. The Effects of TENS, Interferential Stimulation, and Combined Interferential Stimulation and Pulsed Ultrasound on Patients With Disc Herniation-Induced Radicular Pain. Journal of Back and Musculoskeletal Rehabilitation. 2022;35(2):363-71.
15. Hirani DG, Baldha GL. To Compare the Effect of Core Stability Exercise Versus Posterior Pelvic Tilt Exercises on Chronic Low Back Pain. 2019.
16. Elboim-Gabyzon M, Andrawus Najjar S, Shtarker H. Effects of Transcutaneous Electrical Nerve Stimulation (TENS) on Acute Postoperative Pain Intensity and Mobility After Hip Fracture: A Double-Blinded, Randomized Trial. Clinical Interventions in Aging. 2019:1841-50.
17. Nastiti RR, Rahayu UB, editors. Physiotherapy Strategy for Patient With Herniated Disc. Academic Physiotherapy Conference Proceeding. 2021.
18. Divyasree S, Kumaresan A, Vishnuram S. Effect of McKenzie Lumbar Extension Exercise With TENS on Lumbar Radiculopathy. Biomedicine. 2023;43(3):1032-5.
19. Ozsoy G, Ilcin N, Ozsoy I, Gurpinar B, Buyukturan O, Buyukturan B, et al. The Effects of Myofascial Release Technique Combined With Core Stabilization Exercise in Elderly With Non-Specific Low Back Pain: A Randomized Controlled, Single-Blind Study. Clinical Interventions in Aging. 2019:1729-40.
20. McCaffery M, Beebe A. The Numeric Pain Rating Scale Instructions. Pain: Clinic Manual for Nursing Practice. 1989.
21. Fairbank JC, Pynsent PB. The Oswestry Disability Index. Spine. 2000;25(22):2940-53.