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Research Article

Protocol for a Prospective Cohort Study on Determinants of Outcomes in Lumbar Radiculopathy Surgery

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Highlights:

- A prospective cohort study evaluates predictors of surgical outcomes in lumbar radiculopathy.
- NfL, clusterin, and miR-30c-5p are explored as novel blood-based biomarkers.
- Multimodal assessment includes psychological, neurophysiological, and molecular data.
- Findings aim to support personalized treatment strategies for neuropathic pain.

Abstract

Introduction: Lumbar radiculopathies involving the entrapment of nerve roots in the lumbar spine are common neuropathic conditions. These conditions affect 40% to 70% of individuals in their lifetime and lead to significant medical costs.

Materials and Methods: This prospective cohort study, conducted at Hospital Central de la Defensa Gómez Ulla, Madrid (Spain), adheres to the STROBE guidelines. The study includes patients aged 18-75 with lumbar radiculopathy, confirmed by clinical diagnosis, imaging, and electromyography (EMG) findings. Exclusion criteria include previous lumbar spine surgeries and systemic diseases. The primary outcome is the Oswestry Low Back Pain Disability Questionnaire. Sample size calculations determined the need for 141 participants, accounting for a 15% dropout rate.

Procedure: Patients will undergo an initial assessment, including EMG tests, sociodemographic and psychological questionnaires, blood sample tests and physical questionnaires. This process will be repeated six months post-intervention, except for the blood sample test, expectations questionnaire, and EMG, which will be performed only once.

Statistical Analyses: Data will be analyzed using Python statsmodels and pandas libraries, employing a multivariate linear regression analysis. Assumptions of linearity, independence, homoscedasticity, normality, and no multicollinearity will be validated. Corrective measures will be applied if assumptions are violated.

Ethics and Dissemination: The study follows the Declaration of Helsinki guidelines and the Ethics Committee of Universidad Rey Juan Carlos has been approved (070220241052024). Potential risks will be minimized, and adverse events will be recorded and addressed. Findings will be published in high-impact journals and presented at conferences

Keywords: Sciatic Nerve; Lumbar Radiculopathy; NFL, Neuropathic Pain

Introduction

Lumbar radiculopathies involving the entrapment of nerve roots in the lumbar spine stand as one of the most prevalent neuropathic conditions worldwide. In the UK around 40% to 70% of individuals will suffer from this condition at some point in their lives, hence, these ailment accounts for significant medical costs, estimated at £270 million [1] and reaching the $305 million in the USA [2].

NeuPSIG working group has recently redefined radiculopathy as "a lesion or disease of a nerve root or dorsal root ganglia associated with a condition slowing or block" [3], marking a pivotal shift in its understanding.

Lumbar radicular pain, as a primary symptom, typically manifests as back pain radiating to the lower limbs [4]. The term "sciatica" is defined as a common condition related to lumbar radicular pain, but to date no precise definition has been found for its diagnosis, giving rise to varying prevalence rates [5,6].

The diagnosis of these conditions primarily implies neurological evaluations and magnetic resonance imaging (MRI), the latter being the most evidence-supported tool for confirmation [7,8]. However, inconclusive MRI results require supplementary tests like electrodiagnostic assessments [9]. Furthermore, employing Dermatomal Somatosensory Evoked Potentials (DSEPs) offers insights into sensory responses at various spinal levels [10]. In research contexts, Quantitative Sensory Testing (QST) serves as a psychophysical method to quantify sensory experiences [11].

Treatment modalities for lumbar radiculopathies are broadly categorized into conservative and invasive approaches. Conservative treatments, mainly involving physiotherapy and pharmacotherapy are preferred, especially in cases with neuropathic pain [12]. Medications like pregabalin, antidepressants and gabapentin are effective in the short to medium term but pose challenges for long-term use due to potential side effects [13]. Physiotherapy tech-

niques, including mechanical traction [14,15], neural mobilization [16], stabilization exercises, electrotherapy and manipulation [17] yield short- to medium-term benefits in pain relief, strength, and mobility, although their long-term efficacy remains inconsistently proven [18]. A recent meta-analysis, however, points to the high heterogeneity and potential bias in physiotherapy trials [19].

In more severe or persistent cases yielding unresponsive to conservative treatments, invasive procedures like neurosurgical decompression followed by an instrumented posterolateral arthrodesis. Post-surgery, patients often report a rapid alleviation in pain and disability in the short term, but mild to moderate symptoms can persist for up to five years [20]. A significant concern is the incidence of "chronic pain after spinal surgery" (CPSS) ranging from 10-40%, characterized by recurrent pain post-surgery [21]. However, surgery is indicated in the presence of severe or progressive neurological deficits or persistent symptoms that do not respond to conservative treatment [22]. Schmid et al. have observed a lack of knowledge and values to be taken into account when selecting patients for successful surgery [6].

Biomarkers play a crucial role in the diagnosis and clinical management of peripheral nerve-related disorders, traditionally relying on neurophysiological parameters such as nerve conduction studies EMG [23]. They are instrumental in assessing the severity and prognosis of peripheral neuropathies [24]. Among various biomarkers, Neurofilament Light Chain (NfL) is particularly significant. It serves as a prognostic indicator not only in plasma but also in cerebrospinal fluid (CSF), highlighting its versatility across different biological mediums. NfL has proven to be a valuable marker in neurodegenerative [25], inflammatory [23], peripheral nerve diseases, and chemotherapy-induced neuropathy [26]. NfL is a structural element of neurons from central and peripheral nervous system. Damage to axons triggers the release of NfL into the interstitial fluid and eventually into the peripheral blood [27]. Increased levels of NfL are thought to represent axonal degeneration, which could contribute in the development of neurodegenerative disorders [28]. Although this has been reported in different peripheral nerve diseases, there is still a lack of knowledge about traumatic peripheral nerve injuries.

Additionally, microRNA biomarkers, particularly increased plasma miR-30c-5p levels, show potential in predicting the onset of neuropathic pain in chronic peripheral ischemia [29].

Several other proteins have been proposed as molecular markers of disease progression that render insight into the pathogenesis of the condition. Amongst them clusterin has been described to be significantly reduced in patients suffering from several painful conditions such as degenerative scoliosis [30], carpal tunnel syndrome, chronic widespread pain [31,32], ostheoarthritis [33] amongst other painful conditions. Moreover, it has been described to return to normal levels once pain relief has been obtained through treatment procedures [30]. This protein provides another variable to assess pain in a less subjective manner and allows to deepen in the molecular mechanisms of pain development providing a further potential therapeutic goal.

Despite the documented presence of NfL in various peripheral nerve diseases, a significant gap remains in the understanding of its role in traumatic peripheral nerve injuries, particularly in how plasma-detected NfL and microRNAs like miR-30c-5p can predict the severity and prognosis of entrapment neuropathies. This gap is compounded by the challenges in identifying patients who might benefit most from surgical intervention.

To address these challenges, our cohort study aims to provide a comprehensive evaluation of prognostic factors related to both NfL and microRNAs, enhancing our understanding of surgical outcomes in lumbar radiculopathies. By systematically collecting and analyzing data from a well-defined patient cohort, we can identify not only clinical indicators but also subjective factors such as pain and patient beliefs. This approach allows for a more nuanced understanding of the elements that influence surgical outcomes, ultimately contributing to more personalized and effective treatment strategies for patients with lumbar radiculopathies.

Material and Methods

The following methodology is presented in accordance with the STROBE guidelines [34]. A prospective cohort study will be conducted in hospitals of the Community of Madrid (Spain). All patients will receive informed consent formularies prior to the enrollment.

The cohort will track patients who meet the inclusion and exclusion criteria from their initial consultation through a follow-up period. For the recruitment of the sample, data will be collected from patients who meet the inclusion and exclusion criteria.

For sample selection, the following inclusion criteria will be considered: 1) age between 18-75 years old; 2) symptoms duration of more than 3 months; 3) clinical diagnosis of lumbar radiculopathy: conduction block along a spinal nerve or nerve root, clinically manifested by sensory loss in a dermatome or myotatic weakness or reflex changes[35]; 4) leg pain in L5 or S1 dermatomes; 5) clinically relevant demonstrable abnormality in imaging studies indicating compression of L5 or S1 nerve roots at the L4-L5 or L5-S1 levels; 6) positive electromyography (EMG) findings; and 7) listed for surgery.

The exclusion criteria will be as follows: 1) sensorimotor deficits of the femoral and/or femoral cutaneous nerve; 2) age greater than 75 or less than 18 years old; 3) previous lumbar spine surgeries; 4) cauda equina syndrome; 5) pregnancy; 6) musculoskeletal comorbidities such as rheumatoid arthritis and/or fibromyalgia; 7) systemic diseases such as diabetes mellitus and/or thyroid diseases; 8) recent chemotherapy treatment; 9) vascular diseases; 10) numbness and/or tingling in the feet preceded or accompanied by sensory alterations in the hands (polyneuropathies); 11) previous diagnosis of chronic or neuropathic pain; and 12) difficulty understanding the Spanish language.

Surgical procedure description

The surgical procedure employed in this study involves a neurosurgical decompression followed by an instrumented posterolateral arthrodesis. This process is accomplished using osteosynthesis with pedicular screws. Initially, neurosurgical decompression is carried out to relieve pressure on the nerve roots. Subsequently, the procedure advances to posterolateral arthrodesis. This technique aims to achieve spinal stability by creating a bony fusion between two or more vertebrae. Instrumentation, in this context, involves the application of pedicular screws, which are strategically placed to secure the vertebrae. These screws provide immediate stability and facilitate the fusion process by maintaining proper alignment and immobilization of the spinal segments involved. This method has demonstrated substantial efficacy in treating various spinal pathologies, ranging from degenerative diseases to trauma-related instabilities [36,37].

Sample description

Sociodemographic information

Sociodemographic data for the cohort will include age, gender, ethnicity, educational level, employment status, marital status, and income level. Age, sex and gender will be recorded. Ethnicity will be categorized based on self-identification. Educational level will be documented according to the highest degree obtained, ranging from no formal education to advanced degrees (e.g., high school diploma, bachelor's degree, master's degree, doctorate). Employment status will include categories such as employed, unemployed, retired, and student. Marital status will be classified as single, married, divorced, or widowed. Income level will be reported in predefined brackets to capture the range of socioeconomic statuses within the cohort.

Psychological variables

Fear-avoidance and catastrophizing: The Spanish version of the Pain Catastrophizing Scale (PCS) will be used to assess the level of catastrophizing. The PCS consists of 13 items, and each item is scored on a scale from 0 to 4. The total score range is from 0 to 52, where higher scores indicate higher levels of catastrophizing. This instrument has demonstrated the same original factorial structure, comprising three factors (rumination, magnification, and helplessness), as well as adequate psychometric properties [38].

To evaluate patients beliefs regarding the effect of physical activity and work on their pain, the Fear-Avoidance Beliefs Questionnaire (FABQ) will be used. The FABQ consists of 16 items, and patients rate their agreement with each item on a seven-point Likert scale (0 = totally disagree, 6 = totally agree) [39,40]. This questionnaire has shown excellent test-retest reliability (CCI = 0.97) in the Spanish validation [39].

To assess fear of movement or (re)injury related to pain, the Tampa Scale of Kinesiophobia (TSK) validated in Spanish will be used. The 11-item version of the TSK, which demonstrated good reliability properties in patients with pain, will be employed. Each item is rated on a four-point Likert scale ranging from "strongly agree" to "strongly disagree." Total scores range from 11 to 44, with

higher scores indicating more fear of movement and/or (re)injury. The minimal detectable change for chronic pain in the English version is 5.6 points [41].

Main outcome

Oswestry Low Back Pain Disability Questionnaire is the gold standard for assessing functional disability in low back pain and has been validated in Spanish. This questionnaire consists of 10 questions with 5 possible responses each [42]. The results are reported as a percentage, with higher percentages indicating greater functional limitation. The questionnaire has a sensitivity of 76% and specificity of 63% for a cutoff point of ≥10 points. Additionally, it has a Cronbach's alpha coefficient of 0.85 and an intraclass correlation coefficient for test-retest reliability of 0.92 [43].

Potential predictors

NfL

NfL concentration in serum samples will be analyzed using a SIMOA immunoassay (Quanterix, Billerica, MA, USA). The sample concentrations will be calculated based on individual standard curves for each analysis using Simoa HD-X software (version 3.1.2011.30002, Quanterix). The coefficient of variation between analyses for the two levels of quality control will be 6.4% and 11.9% [44].

Clusterin

Serum clusterin levels shall be analyzed by immunoassay. Plasma samples shall be thawed and diluted 1:1000 to quantify clusterin concentration by ELISA (EHCLU kit, Thermo-Fischer Scientific, Frederick, MD, USA) following the manufacturer's instructions [45].

MicroRNA-30c-5p

For microRNA-30c-5p measurement, RNA extraction utilized the RNeasy Mini Kit (Qiagen, Venlo, Netherlands), adhering to the manufacturer's guidelines. RNA purity and concentration were assessed using a NanoDrop 2000 spectrophotometer (Thermo Fisher Scientific, Waltham, MA, USA), with a 260/280 nm absorbance ratio confirming integrity. cDNA synthesis was conducted from 5 ng of total RNA for each DRG side, using PrimeScript™ RT Master Mix (Perfect Real Time) (Takara Bio Inc., Shiga, Japan), according to the manufacturer's instructions. qPCR amplification was performed with TB Green® Premix Ex Taq™ (Tli RNaseH Plus) (Takara Bio Inc., Shiga, Japan). The differentially expressed miRNAs we will be looking for are as follows [29].

Electromyography (EMG)

The EMG procedure will involve the placement of a disposable needle electrode in the affected muscles, depending on the compromised nerve root and its corresponding myotomes, to assess their bioelectrical activity. Measurements will be carried out on sensory nerve conduction velocity (m/s), distal motor latency (ms), sensory nerve action potential (SNAP) (mV) and compound motor action potential (CMAP) (mV) based on the protocol by Paige C. Roy., *et al*. [46].

Neurological exam

The patellar and Achilles reflexes will be evaluated to observe possible reduction or attenuation [47].

A muscular balance assessment will be conducted, evaluating the strength of dorsiflexors, plantar flexors, knee flexors, and knee extensors using the Daniels scale [48].

Neuropathic pain

The Pain DETECT questionnaire will be used for the identification and detection of neuropathic pain compared to other types of pain, with particular attention to the presence of back pain. This questionnaire consists of 4 sections and has been validated in Spanish. It includes the Visual Analog Scale (VAS) and a body diagram to help localize and quantify pain. The Pain DETECT has a Cronbach's alpha coefficient of 0.86 and an intraclass correlation coefficient for test-retest reliability of 0.93. For a cutoff point of ≥17 points, it has a sensitivity of 75% and specificity of 84% [49].

Pressure pain threshold (PPT)

PPT is defined as the minimum amount of pressure required to cause pain. Algometry has been described as highly reliable for measuring pressure pain threshold (ICC = 0.91, 95% CI 0.82-0.97) [50]. PPT will be performed using a digital algometer (Model FDX 10®, Wagner Instruments, Greenwich, CT, USA). This instrument measures pressure in kilograms, with the pain threshold expressed in kg/cm^2. In the protocol, the patient will indicate when he/she first experiences the onset of pain, at which time the pressure will

be stopped and recorded. Three measurements shall be taken, with an interval of 30 seconds between each measurement to avoid a temporal summation effect. The measurement shall be taken at a point located at the L5 dermatome bilaterally, as well as at the region of greatest pain indicated by the patient. The mean of the three measurements shall be calculated.

Temporal summation

Induced temporal summation is the increase in C-fiber evoked responses by neurons in the dorsal horn of the spinal cord due to activation of C-fibers by repeated high frequency stimuli [51]. The measurement of temporal summation is mechanical. The Pinprick stimulator set (MRC Systems GmbH Heidelberg, Germany) is used. Pain perception is compared using the VAS for two types of stimuli: a single sharp stimulus and a train of 10 sharp stimuli with the same force (256Nm), applied to the midpoint of the L5 dermatome and the area of greatest pain reported by the patient at a repetition frequency of 1Hz. Both stimuli are applied over an area of 1 cm2. The stimuli are alternated five times within the predefined area. The ratio is calculated by dividing the average pain produced by the stimuli in train by the pain produced by the single stimulus. This method has been used and validated in several studies on temporal summation. In this study, the measurement will be performed before and after treatment [52].

Mechanical detection thresholds

Mechanical detection thresholds will be obtained using von Frey filaments. They shall be applied perpendicular to the skin at a point in the L5 dermatome region for 1 second, and each filament shall be applied three times in ascending order. The smallest filament that elicits a pressure sensation shall be considered the detection threshold and shall be used to measure the patient's sensitivity, pain and allodynia [53].

Vibration detection threshold

The vibration threshold shall be obtained using a tuning fork with a vibration frequency of 64 Hz and a scale of 8/8. To verify the threshold values, the struck and vibrating tuning fork is placed in the test area, if possible, over a bony eminence. The test subject indicates when he/she stops feeling the vibration of the tuning fork. The intensity of the stimulus is then plotted on the tuning fork scale. After a threefold determination of the vibration detection threshold, the arithmetic mean value of the thresholds can be calculated [54].

Expectations

Patients will be given a pre-intervention survey requesting expectations for treatment. In this survey the patient will be given 5 possible answers to discuss their expectations for the success of their treatment: "definitely yes", "yes", "not sure", "no" and "definitely no". The questions to be asked to the patient will be the following [55].

- Complete relief of symptoms (pain, stiffness, numbness, weakness, stability).
- Moderate relief of symptoms (pain, stiffness, stiffness, numbness, weakness, stability)
- To perform more domestic activities.
- To sleep more comfortably.
- To return to my usual work
- Exercise and more recreational activities.
- Prevent future disabilities.

Procedure

After the primary selection of subjects by physicians, patients will be informed about the study characteristics. During this meeting, the voluntary nature of their participation will be explained, and they will be informed that they can withdraw from the cohort at any time. They will also be informed that refusing to participate will not negatively impact their treatment or scheduled follow-up with their physician.

The researcher in charge will register any dropouts or treatment failures. To prevent dropouts, one of the researchers will make phone calls to reassess and remind patients of their upcoming appointments. On the assessment day, patients will undergo all the tests and measurements described in the subsequent section on variables. The procedure will be as follows

Within 2 weeks prior to the visit, the patient will undergo an EMG test. During the visit, patients will complete all the sociodemographic, psychological, and predictor questionnaires. After filling out the forms, the participant will undergo the following tests: mechanical detection thresholds, pressure pain threshold assessment, conditioned pain modulation, and temporal summation assessment.

At the end of the tests, the participants will go to another room where a nurse from the center will take a blood sample that will be

analyzed by a professional in the laboratory. A peripheral venous blood sample (10 ml) will be collected in an EDTA tube. Thirty minutes after collection, plasma will be separated by centrifugation at 1000g for 10 minutes at 4ºC. The plasma will be transferred to a 2mL Eppendorf and stored at -80ºC until processed.

This process of predictive tests will be repeated six months after the intervention, except for the blood sample, expectations, and EMG, which will only be performed at the first session.

Sample size

Sample size was calculated using *Python version 3.12.3* with *scipy. stats* library. In this study, the primary outcome is the Oswestry Low Back Pain Disability Questionnaire, with nine predictor variables, five of which are measured only once and four that are measured at two different time points. To determine the appropriate sample size, we set the significance level at 0.05 and the desired power at 0.80, with an effect size of 0.35. Using a two-tailed test, the critical values for the significance level and power were calculated. For the predictors measured at multiple time points, an intra-class correlation (ICC) of 0.5 was assumed, resulting in a design effect of 2.5. The initial sample size calculation using multiple linear regression formula and the total number of predictors yielded a sample size of 75. After adjusting for the design effect for the repeated measurements, the sample size increased to 113. Finally, accounting for an expected dropout rate of 15%, the required sample size was determined to be 141 participants.

Statistical analyses

The data will be analyzed using *Python version 3.12.3*, utilizing the *statsmodels* and *pandas* libraries. Before fitting the regression models, key assumptions will be validated: linearity between the dependent and independent variables, independence of observations, homoscedasticity, normality of residuals, and no perfect multicollinearity among predictors. Diagnostic tests and plots will be used to check these assumptions: scatter plots for linearity, the Durbin-Watson test for autocorrelation, residual plots and the Breusch-Pagan test for homoscedasticity, and the Shapiro-Wilk test and Q-Q plots for normality. Variance inflation factors (VIF) will assess multicollinearity.

If assumptions are violated, corrective actions will be taken adding polynomial or interaction terms for non-linearity, using time series models or generalized least squares for autocorrelation, applying robust standard errors or transforming the dependent variable for heteroscedasticity, transforming data for non-normal residuals, and addressing multicollinearity by removing or combining predictors or using regularization techniques like ridge regression or lasso.

Results will be reported as regression coefficients with 95% confidence intervals and p-values, with significance set at $p < 0.05$. The adjusted R-squared value will assess model fit. Sensitivity analyses will examine the robustness of findings, including excluding outliers and using alternative ICC values. All analyses will be interpreted considering clinical and statistical significance.

Discussion

Predictive models have become essential tools for assessing and anticipating the success of treatments across various areas of medicine. Based on clinical data—such as sensory, physical, demographic, psychological information, and biomarkers—these models make it possible to identify patterns and trends that help predict a patient's response to specific therapeutic interventions. However, many current models present limitations that hinder their clinical applicability, as highlighted by the systematic review by Wynants., *et al*. [56]. One such limitation is particularly evident in the field of neuropathic pain, where the lack of an objective measurement method complicates diagnosis and the selection of effective treatments. This underscores the need to develop objective and quantifiable tools, among which blood-derived biomarkers emerge as promising candidates. These biomarkers—genetic, neurophysiological, or molecular in nature—could not only facilitate diagnosis but also assess the effectiveness of therapies and predict individual treatment responses [57,58]. Their integration into predictive models would pave the way for more personalized pain medicine, reducing trial and error, lowering costs, and enhancing patient experience [59].

Among the potential biomarkers is NfL, which, despite limited evidence due to the lack of representative reference values to account for physiological increases—values that may also vary with patient age [60] appears to be a promising blood biomarker for evaluating nerve damage in patients with peripheral polyneuropathy [61,62]. Elevated plasma levels of NfL have been observed in

comparison to healthy individuals, suggesting its potential as a marker of neuronal injury. This overexpression has been widely documented in metabolic, inflammatory, or hereditary diseases such as diabetic polyneuropathy and Charcot-Marie-Tooth disease [60]. However, its application in traumatic injuries and entrapment neuropathies remains an emerging field [61,63].

In recent years, interest has grown in using these biomarkers as prognostic factors in various pathologies [64]. The influence of NfL has been studied in the progression of diseases related to the central nervous system [65,66], and even in infectious pathologies [66], though there is less evidence regarding its role in traumatic conditions. One area that requires further research is its utility as a predictor of neuropathy severity and postoperative progression. In this regard, some studies have shown a positive correlation between plasma NfL levels and the degree of nerve damage in patients with lumbar radiculopathies [68]. This may suggest that the biomarker could play a relevant role in evaluating treatment response. Nevertheless, additional studies are needed to determine its applicability in clinical practice, particularly in monitoring patients who undergo nerve decompression surgery or peripheral nerve repair [69].

This study aims to address this knowledge gap by evaluating the utility of NfL as a predictor of therapeutic success following surgery and, consequently, its potential use as an indicator of responders and non-responders to surgical interventions. If a positive association is found, further research will be needed to determine its diagnostic accuracy, temporal patterns, and prognostic value in other conditions.

In this way, the incorporation of biomarkers such as NfL into clinical practice could complement traditional clinical criteria, offering an objective assessment of nerve involvement and improving the identification of patients who would truly benefit from an intervention. This tool would not only enable earlier and more precise detection of neurodegenerative processes but also allow for more dynamic monitoring of neuronal damage progression over time. Furthermore, its use could optimize therapeutic decision-making, enabling more personalized, biologically-informed medicine, ultimately contributing to better clinical outcomes and more efficient healthcare resource management.

Ethics and Diffusion

Ethics

The study will be conducted in accordance with ethical procedures for medical research involving human subjects, following the guidelines of the Declaration of Helsinki, as adopted by the 18th World Medical Assembly [70] and its subsequent revisions, including the revised version from the 63rd Assembly [70]. The study has been approved by the Ethics Committee of Universidad Rey Juan Carlos (070220241052024).

Risks and safety measures

Potential risks associated with the study will be minimized through stringent safety measures. A dedicated record of all adverse effects reported by patients during treatment sessions or re-evaluations will be maintained. Participants will be monitored closely, and any adverse events will be promptly addressed according to established medical protocols. The safety and well-being of participants will be a top priority throughout the study.

Communication of Findings

Upon completion of the study, a comprehensive statistical analysis of the results will be performed. The findings will be prepared for publication to contribute to the body of knowledge in the field of pain and rehabilitation. Additionally, selected results will be presented at national and international conferences, ensuring wide dissemination among the scientific community and healthcare professionals. The communication strategy will also include providing feedback to study participants and collaborating institutions, reinforcing the study commitment to transparency and knowledge sharing.

Conflict of Interest

Nothing to declare.

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