Observational Study

Predicting Responses to Interventional Pain Management Techniques for Chronic Low Back Pain: A Single-Center Observational Study (PReTi-Back Study)

Santiago Garcia-Hernandez, MD[1], Fernando Higuero-Cantonero, MD[1], Francisco de la Gala Garcia, MD, PhD[1], Ángel Alonso Chico, MD[1], Javier Blanco Aceituno, MD[1], Sara Zapatero Garcia, MD, PhD[1], José Laureano Aguilar Godoy, MD[1], Javier Hortal Iglesias, MD, PhD[1], Ana Esther Lopez Perez, MD, PhD[1], and Ignacio Garutti, MD, PhD[1-3]

From: [1]Department of Anesthesiology, Critical Care, and Pain Medicine, Chronic Pain Unit, Gregorio Marañón University General Hospital, Madrid, Spain; [2]Department of Pharmacology, School of Medicine, Complutense University of Madrid, Madrid, Spain; [3]Foundation for Biomedical Research of the Gregorio Marañón Hospital (FIBHGM), Madrid, Spain

Address Correspondence: Santiago Garcia-Hernandez, MD Calle del Dr. Esquerdo, 46 28007, Madrid, Spain E-mail: sgarciahernandez@salud.madrid.org

Disclaimer: There was no external funding in the preparation of this article.

Conflict of interest: Each author certifies that he or she, or a member of his or her immediate family, has no commercial association (i.e., consultancies, stock ownership, equity interest, patent/licensing arrangements, etc.) that might pose a conflict of interest in connection with the submitted article.

Article received: 01-18-2024
Revised article received: 05-21-2024
Accepted for publication: 06-10-2024

Free full article: www.painphysicianjournal.com

Background: Exploring factors linked to the outcomes of certain interventional pain management techniques may optimize the selection of candidates for those procedures. Our hypothesis is that factors that influence responses to interventional therapies for chronic low back pain (CLBP) can be identified by analyzing a prospective cohort.

Objectives: Our main aim is to identify the factors that may be associated with adult patients' responses to interventional therapies for the treatment of CLBP after 4 weeks of follow-up. Secondary objectives include the development of a predictive model and the establishment of a predictive score.

Study Design: The PReTi-Back (Predicting REsponse to interventional Therapies In chronic BACK pain) study is an observational prospective single-center study, employing a nonprobability-sampling method.

Setting: Our population consists of adult outpatients with CLBP in a chronic pain unit of a tertiary hospital. The procedures we evaluated included epidural steroid injections, medial branch blocks and denervations, dorsal root ganglion blocks, and pulsed radiofrequency.

Methods: Ratings on the Numeric Pain Rating Scale (NPRS) and Oswestry Disability Index (ODI) were measured at the baseline and after 4 weeks of follow-up. The primary outcome of the study was composite and was evaluated at 4 weeks. A positive response to an intervention was defined as the simultaneous occurrence of a decrease of at least 2 points in the NPRS score and a decrease of at least 20% in the ODI score. A predictive model was constructed using logistic regression analysis, which incorporated 14 variables selected in advance. A predictive score was developed based on the odds ratios of the model variables.

Results: Four hundred patients were recruited. Of these patients, 368 completed follow-up, 49 were excluded, and 319 were included in the analysis. The interventional therapies provided a positive response to 85 patients (26.6%) at 4 weeks. Listhesis, radicular compression, and satisfaction with previous interventional therapies were positively associated with the positive response, and their ORs were close to 2. Meanwhile, obesity and persistent spinal pain syndrome type 2 (PSPS-2) had negative associations with the outcome, presenting ORs close to 0.5. The models were statistically significant and exhibited satisfactory goodness of fit. The area under the curve was 0.67 (95% CI, 0.60-0.74). Both models exhibited low sensitivity but high specificity. The synthesis of the prediction score had little impact on its discriminatory capacity.

Limitations: The subgroup analysis revealed that both listhesis and radicular compression were associated with the response to epidural therapies but not with the response to medial branch therapies. The score was efficient in ruling out those who would not benefit from intervention (scores of 0 or one), but its main limitation was that it was less effective in identifying those who might respond favorably (scores ≥ 2).

Conclusions: Patients satisfied with previously performed interventional therapies or who exhibit findings of radicular compression or listhesis on imaging show approximately twice the likelihood of experiencing a positive response to short-term IMPT than do patients without those characteristics. Patients who are obese or have PSPS-2 exhibit approximately a 50% lower likelihood of short-term response than do patients without these conditions.

Key words: Chronic low back pain, interventional pain management, predictive factors, epidural injections, medial branch therapies, treatment response, logistic regression, predictive model, outcome assessment, tailored medicine

Pain Physician 2024: 27:E851-E863

Low back pain has an estimated annual prevalence between 20% and 40% (1-5) and is the leading cause of years lived with disability (YLD) in most countries (6).

The correct way to manage chronic low back pain (CLBP) differs depending on the condition's etiology (7-10), the patient's characteristics and preferences, and the availability of resources (11-14). Interventional pain management techniques (IPMTs) target specific structures presumably involved in the production, transmission, or processing of the nociceptive signaling (15). IPMTs are limited by their costs and potential risks. Cost-effectiveness analyses in the United States (US) revealed that the average cost of a quality-adjusted life year for a CLBP patient was $3,300-$5,400 in lumbar facet joint nerve interventions and epidural injections (16-18). Low adverse event rates have been described for IPMTs, but a central steroid response and a transient incremental pain increase are both reported in 2% of patients (19). Exploring factors linked to IPMT outcomes could optimize the selection of candidates for these techniques, improving efficacy and benefit/harm ratio and leading to more rational resource utilization (20-25).

The hypothesis of this study is that factors influencing responses to IPMTs for CLBP treatment can be identified through the analysis of a prospective cohort.

Objectives

The main aim of this study is to identify the factors that may be associated with clinical responses to IPMTs for the treatment of CLBP in adult patients after 4 weeks of follow-up. The secondary objectives include the development of a predictive model and the establishment of a scoring system derived from this model.

Methods

Study Design

The PReTi-Back (Predicting REsponse to interventional Therapies In chronic BACK pain) study is an observational prospective single-center study that employs a non-probability-sampling method. The STROBE guidelines were followed in this report (26). Informed consent to participation was obtained from every patient.

Setting

The PReTi-Back study received the approval of the Pharmacological Research Ethical Committee of Gregorio Marañón University General Hospital and was granted the approval number of IORG0005055. The protocol of the study was registered at www.clinicaltrials.gov under the identifier NCT04451252 (27). The recruitment period was opened between October 2nd, 2019 and March 10th, 2020 and again between July 3rd, 2020 and July 4th, 2021. (Recruitment was split due to the COVID-19 pandemic.)

Patients

Our population consisted of adult outpatients with CLBP in the chronic pain unit of our hospital.

To meet the inclusion criteria, patients needed to be over 18 years of age, have CLBP, and have been indicated for one of the following IPMTs: therapeutic facet joint nerve block (TFJNB) and neurotomy (RFNFJ), interlaminar lumbar epidural injection (ILEI), caudal epidural injection (CEI), or dorsal root ganglion injection (DRGI) and pulsed radiofrequency (PRFDRG). Exclusion criteria for patients were: not having undergone the IMPT, an unwillingness to participate, being impossible to obtain response data for, having received back surgery any time during the study, and suffering from any intercurrent disease that might have interfered with the evaluation of chronic lumbar pain.

Once scheduled for an IPMT, patients were recruited at the office or telephonically (during the COVID-19 pandemic). This visit was designed "visit 0 (V0)." A telephone follow-up visit was carried out 4 weeks after the IPMT was performed and was designated "4-week visit (V4W)."

Variables

In our chronic pain unit, a set of clinical and ra-

diological criteria is utilized to diagnose the etiology or pain syndrome in patients with CLBP. Table 1 encapsulates both the diagnostic parameters and the corresponding IPMTs indicated for each diagnosis.

The procedural details of the IPMTs included in this study are summarized in Table 2, which were indicated and performed in line with current guidelines (15,28-30).

Pain intensity was measured with a Numeric Rating Scale (NRS-11). The NRS-11 is an 11-point scale on which patients rate the intensity of their pain from 0 ("no pain") to 10 ("worst pain imaginable") (31-33). Disability related to CLBP was estimated with a validated Spanish translation of the original 1980 version (v1.0) of the Oswestry Disability Index (34).

The primary outcome of the study was composite and was evaluated at 4 weeks. A positive response (PR) to an IPMT was defined as the simultaneous occurrence of a decrease of at least 2 points in the Numeric Pain Rating Scale (NPRS) score and a decrease of at least 20% in the ODI score.

Fourteen candidate variables were selected for analysis in the predictive model. The decision to include these specific variables was guided by literature and clinical experience. Those were: sick leave from work, depression or anxiety, obesity, existence of other chronic pain, persistent spinal pain syndrome type 2 (PSPS-2), radicular compression in imaging, listhesis in imaging, herniated disk in imaging, pain radiating to the lower limb below the knee, age over 65 years

Table 1. *Diagnostic Criteria and Indication of Interventional Pain Management Techniques*

Diagnosis	Criteria
Disc Herniation - Radiculitis	Clinical: pain radiating from the lower back down to the leg with dermatomal distribution, typically exhibits neuropathic characteristics; may be accompanied by numbness, tingling, or muscle weakness; Lasègue sign. Imaging: evidence of impingement on a nerve root, caused either by disc herniation, or other causes such as spondylolisthesis, spondylolysis, or facet joint cysts resulting in foraminal or lateral recess stenosis. Electromyography findings are also considered. IPMT: first line ILEI Vs. DRGI (if positive EMG findings); CEI (when ILEI or DRGI were technically not feasible); PRFDRG (when the duration of relief from DRGI was unsatisfactory).
Lumbar Facet Joint Pain	Clinical: pain localized in the lumbar region, often exacerbated by hyperextension and lateral rotation of the spine; mechanical pain; morning stiffness; may refer pain to the buttock or thigh; absence of neurological deficits; diagnostic relief from medial branch nerve blocks indicating facet joint origin of pain. Imaging: may demonstrate facet joint arthropathy but primarily used to rule out other conditions. IPMT: TFJNB (first line); RFNFJ (second line).
Spinal Stenosis	Clinical: pain and/or cramping in the lower back and legs, especially when standing or walking for extended periods; symptoms relieved by sitting or lumbar flexion. Imaging: supporting evidence of spinal stenosis. IPMT: ILEI (first line); CEI (when ILEI was technically not feasible)
Axial – Discogenic Pain	Clinical: centralized lumbar pain without significant radiation; exacerbated by activities that increase intradiscal pressure such as sitting, lifting or Valsalva maneuvers; relief with recumbency; no sensory or motor deficits attributable to one specific nerve root. Imaging: annular tears or disc degeneration on imaging, Modic changes type 1. IPMT: ILEI (first line); CEI (when ILEI was technically not feasible).
Post-surgery Syndrome (PSPS-2)	Clinical: chronic pain in the back and/or legs that persists or recurs after spinal surgery. May be due to scar tissue (epidural fibrosis), nerve root entrapment, adjacent segment disease, recurrent disc herniation or unresolved underlying pathology. Imaging: lack of signs of spinal instability in imaging *. IPMT: first line ILEI Vs. DRGI (if positive EMG findings); CEI (when ILEI or DRGI were technically not feasible); PRFDRG (when the duration of relief from DRGI was unsatisfactory); TFJNB (first line when facet joints were deemed the primary source, adjacent segments were targeted in patients with lumbar instrumentation); RFNFJ (second line when facet joints were deemed the primary source)
Chronic Low Back Pain of Unknown Etiology	Clinical: low back pain that eludes diagnosis after a comprehensive medical evaluation; pain that does not follow a typical pattern or anatomical distribution and for which specific structural or pathological sources have not been identified. Imaging: no definitive pathology that corresponds with the patient's pain symptoms. IPMT: ILEI; CEI (when ILEI was technically not feasible)

ILEI: interlaminar lumbar epidural injection; TFJNB: therapeutic facet joint nerve block; CEI: caudal epidural injection; RFNFJ: radiofrequency neurotomy of the facet joint; PRFDRG: pulsed radiofrequency of the dorsal root ganglion; DRGI: dorsal root ganglion injection; PSPS-2: persistent spinal pain syndrome Type 2. * these patients are referred to a Spine Surgeon.

Table 2. *Procedure Details of Interventional Pain Management Techniques (IPMT).*

IMPT	Projections, landmarks and target	Confirmation method	Medication or Radiofrequency applied
Interlaminar Lumbar Epidural Injection	Paramedian approach, AP and lateral; Interlaminar space	Loss of resistance, epidural spilling of contrast agent	17-G Tuohy needle Mix 3 mL Ropivacaine 0.2% + Betamethasone ph 6 mg + 2 mL saline
Caudal Epidural Injection	Sacral hiatus palpation; AP and lateral; sacral canal	Loss of resistance, satisfactory contrast dispersion	17-G Tuohy needle Mix 7 mL Ropivacaine 0.2% + Betamethasone ph 6 mg + 7 mL saline
Therapeutic Facet Joint Nerve Block	AP, oblique*, lateral; Medial branch of the dorsal ramus	Fluoroscopic positioning	22-G Quincke needle. Mix 3 mL Ropivacaine 0.2% + Triamcinolone 40mg; 1 mL per nerve.
Dorsal Root Ganglion Injection	Supraneural approach; Oblique†, lateral, AP;	Fluoroscopic positioning, satisfactory contrast dispersion	20 G Coudé ® blunt needle 1 mL Ropivacaine 0.2% + Betamethasone 3 mg
Radiofrequency Neurotomy of Facet Joint	AP, oblique*, (10-20º), lateral; Medial branch of the dorsal ramus	Fluoroscopic positioning; 200-500 Ω; Sensitive stimulation: 50 Hz, 1 ms, 0.6 V; Motor response check: 2 Hz, 2 ms twice the voltage that produced sensitive response	18-G needles. RF Ablation: 90 sec, 80ºC.
Pulsed Radiofrequency of Dorsal Root Ganglion	Oblique (10-20º), lateral, AP; Kambin's triangle	Fluoroscopic positioning; 200-500 Ω; Sensitive stimulation: 50 Hz, 1 ms, 0.6 V; Motor response check: 2 Hz, 2 ms twice the voltage that produced sensitive response	22-G injection electrode Pulsed RF: 4 min, 42ºC

In all techniques, the patient was in the prone position. Skin was disinfected and the procedure was conducted under aseptic conditions An anteroposterior (AP) fluoroscopic projection of the lumbar spine was obtained, and the T12-L1 level was identified to rule out anomalies of the lumbosacral transition. Subsequently, the target intervertebral level was identified, and the craniocaudal angulation was adjusted to square the superior endplate. All patients underwent the technique on an outpatient basis. Oblique*: "Scotty dog", 20-30º; Oblique†: superior articular process between anterior and posterior edge of vertebral body, base of the articular process in line with the pedicle; Contrast Agent: Iohexol 300 mg/mL Omnipaque ® GE HealthCare ® 100 mL bottle; Mepivacaine 1% B.Braun ® 10 mL ampule; Bupivacaine 0.25% Physan ® 10 mL ampule; Triamcinolone 40 mg Trigon Depot ® Bristol Myers Squibb ® IPMT 1 mL vial; Bethametasone phosphate 6 mg Celestone Cronodose ® Organon ® 2 mL vial; Radiofrequency device: Cosman G4 RF ® (Boston Scientific ®); 17-G Tuohy needle 90 mm Vygon ®; 22-G Quincke needle 90 mm Becton Dickinson ®; 20-G 114 mm Coudé ® Blunt Nerve Block Needle Epimed ®, 22-G Injection Electrode 100 mm Unified ™ BostonScientific ®. Interventional Pain Management Technique; PSPS-2: Persistent Spinal Pain Syndrome Type 2; AP: Anteroposterior; RF: Radiofrequency; DRG: Dorsal Root Ganglion; ms: millisecond; Hz: Hertz; mL: milliliter; G: gauge; ºC: degrees Celsius; s: seconds; mg: milligram; Ω: Ohms.

old, chronic therapy with opioid medication, chronic therapy with opioid medication and gabapentinoids, basal ODI ≥ 40 points, and satisfaction with a previously performed IPMT.

Data Sources

Before recruitment, all patients were evaluated by a pain specialist who conducted a thorough anamnesis and physical examination, reviewed imaging findings, and indicated an IPMT. Patient demographics, clinical data, some predictive factors, and outcome-related measurements were gathered or retrieved during visit 0. The rest of the predictive factors, imaging findings, IPMT details, and NPRS and ODI scores were registered on the follow-up visit by a blinded investigator.

Bias

We tried to minimize selection bias during recruitment by ensuring that it was done afterward and independently of the indication of the IPMT. Because we anticipated a significant dropout rate in the telephonic follow-up, multiple calls were conducted on different days and time slots to mitigate potential selection bias. To address potential information bias, particularly in pain self-assessment, this study used validated scales to measure 2 dimensions of the pain experience and then defined a composite primary outcome. Performing the basal interviews after the IPMTs were indicated might have reduced the possibility that the patients had reported higher pain scores to merit IPMTs.

Study Size

The sample size was determined according to the "one in 10 rule," which recommends a minimum of 10 events per candidate predictive factor (35-38). Based on an estimated event occurrence of 45% and a projected loss to follow-up of 25%, we aimed to recruit 400 patients to obtain 300 patients who were not lost to follow-up. Doing this would yield 140 events, allowing for the analysis of up to 14 potential factors.

Quantitative Variables

Continuous variables were tested for normality with the Kolmogorov-Smirnov test. The variables that followed the normal distribution were expressed as mean and standard deviation, whereas median and interquartile range were used for the variables that did not.

Statistical Methods

All data were recorded using an anonymized electronic case report form (E-CRF). For data management, Microsoft Excel version 16.66.1 (Microsoft) for Mac was employed. Statistical analysis was performed with IBM SPSS Statistics version 28.0.1.1 (IBM Corporation) for Mac. For the bootstrap section, Stata software version 17 (StataCorp) for Windows was used.

Only patients who completed the follow-up were included in the analysis. If a variable was missing, it was assumed to be absent.

A logistic regression was employed to develop the predictive model based on the 14 a priori selected variables. The positive response at 4 weeks was used as the dependent variable in the model.

Statistical significance was set at $P < 0.05$ for models and $P < 0.1$ for variables within. To simplify the predictive models, an automated variable selection method was chosen: a backward elimination method based on the Wald statistical index. The specified entry and exit criteria for variables were set at $P < 0.05$ and $P > 0.1$, respectively. The resulting model is referred to as the simplified model.

To assess and compare the performance of the model, calibration and discrimination analyses were conducted. The model calibration utilized the Hosmer-Lemeshow goodness-of-fit test, with significance set at $P < 0.05$. The discriminative ability of the model was examined using receiver operating characteristic (ROC) curves and by calculating the area under the curve (AUC). Sensitivity and specificity were computed based on the classification tables.

Given the inherent variability in responses to different IPMTs, we anticipated the possibility that the nature of the intervention itself could impact the predictors of success. To explore this aspect comprehensively, a subgroup analysis based on distinct intervention categories was performed.

The model's robustness was assessed through bootstrap analysis. One hundred bootstrap samples were generated from the original training dataset through the method of sampling with replacement. In each simulation, a logistic regression model was fitted using the corresponding bootstrap sample. The performance of each fitted model was assessed using AUC, classification error, and other model quality indicators. Additionally, variable selection was tracked across the bootstrap simulations.

Through the use of the odds ratios (ORs) of the variables included in the model, a prediction rule was developed. The performance of the prediction rule was compared with that of the original model. Finally, possible cutoff points for the prediction rule were investigated.

Results

Patients

There were 1080 eligible patients during the recruitment period. Four hundred of those patients were recruited. There were 32 patients (13.3%) lost to follow-up. Three hundred sixty-eight patients completed follow-up. Forty-nine patients were excluded from the study. Three hundred nineteen were included in the analysis (Fig. 1).

Descriptive Data

The main characteristics of the cohort are presented in Table 3. The majority of the patients were women (63.9%), and the candidates' median age was 60 years (IQR 20).

Among the 14 candidate variables, only the 3 related to imaging exhibited missing values in the recorded data. Two hundred seventy-three patients received lumbar MRI scans, 17 patients received CT lumbar spine scans, and 8 received lumbar spine x-rays. There were 21 patients for whom an imaging study could not be retrieved. Imaging-related findings are summarized in Table 4.

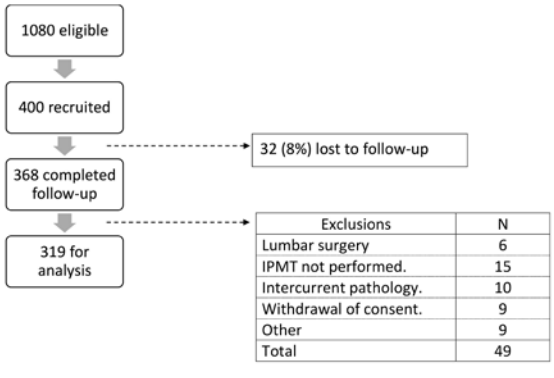

Fig. 1. *Study flow diagram. V4W: visit 4 weeks after the interventional pain management technique was performed; IPMT: Interventional Pain Management Techniques.*

Table 3. *Demographics and clinical characteristics of the cohort.*

		Total
Anthropometry	Female	204 (63.9)
	Age	69 (20)
	Weight	75 (20)
	Height	165 (15)
	BMI	27.4 (6.4)
Civil status	Married/coupled	215 (67.4)
	Divorced	39 (12.2)
	Single	33 (10.3)
	Widowed	32 (10.0)
Specialist referal	Orthopedic surgery	193 (60.5)
	Neurosurgery	94 (29.5)
	Rehabilitation	16 (5)
	Other	16 (5.0)
Working status	Retired	111 (34.8)
	Working	105 (32.9)
	Sick leave/incapacity	103 (32.3)
Comorbidities	Other chronic pain condition	103 (32.3)
	PSPS-2	74 (23.2)
	Osteoarthosis	46 (14.4)
	Obesity	46 (14.4)
	Anxyety or depression	43 (13.5)
	Fibromyalgia	21 (6.6)
	Substance abuse	11 (3.4)
	Osteoporosis	11 (3.4)
	Oncologic disease	11 (3.4)
	Inflammatory reumathic disease	9 (2.8)
	Charlson Comorbidity Index	2 (3)
Signs and synthoms	Lower limb radiated pain	253 (79.3)
	Mechanical pain	146 (45.8)
	Neuropathic pain	145 (45.5)
	Lasègue sign	101 (31.7)
	Neurogenic claudication	45 (14.1)
Home medication	Opioids (oral or transdermal)	225 (70.5)
	Gabapendinoids	173 (54.2)
	Paracetamol	153 (48.0)
	Gabapendinoids + opioids	141 (44.2)
	NSAIDs	133 (41.7)
	Benzodiazepines	45 (14.1)
	Corticosteroids	6 (1.9)

Numerical variables are represented by median and interquartile range. Categorical variables are represented by total number and percentage. PSPS-2: Persistent Spinal Pain Syndrome type 2; NSAIDs: non steroidal anti-inflammatory drugs.

The predominant procedure was interlaminar lumbar epidural injection, which accounted for 55.8% of cases, involving 178 patients. TFJNBs were performed on 52 patients (16.3%), RFNFJs were given to 22 patients (6.9%), and CEI encompassed 16.0% of the group at 51 patients. DRGIs and PRFDRG were performed the least often, at 5.0% (16 patients).

Outcome Data

The IPMTs provided a positive response (as defined above) to 85 patients (26.6%) at 4 weeks. At the beginning of the study, patients presented with an average NPRS score of 8.01 points (95% CI, 7.86-8.16). In the follow-up visit 4 weeks later (V4W), a mean reduction of 1.48 points (95% CI, 1.22-1.74) in NRS-11 was observed, resulting in a score of 6.52 points (95% CI, 6.26-7.79). The initial ODI score was 48.47 points (95% CI, 47.06-49.88). This scale showed a mean reduction of 7.0 points (95% CI, 5.38-8.60), corresponding to an absolute value of 41.56 points (95% CI, 39.63-43.51) in the moment. Both score

Table 4. *Primary findings from the imaging studies.*

Diagnosis	n (%)
Alineation changes	
Listhesis	62 (21.4)
Scoliosis	41 (14.1)
Straightening of the lordosis	25 (8.6)
Vertebral body changes	
Modic type 1	38 (13.1)
Modic type 2	28 (9.7)
Vertebral fracture	14 (4.8)
Modic type 3	1 (0.3)
Posterior elements changes	
Facet joint arthropathy	185 (63.8)
Ligamentum flavum hypertrophy	78 (26.9)
Epidural fibrosis	19 (6.6)
Facet joint synovial cyst	5 (1.7)
Disc changes	
Disc herniation	202 (69.7)
Disc degeneration	170 (58.6)
Bulging disc	98 (33.8)
Annular fissure	15 (5.2)
Nerve root compression	94 (32.4)
Spinal stenosis	
Central stenosis	121 (41.7)
Congenital central stenosis	8 (2.8)

Percentage is calculated over number of patients with either Lumbar MRI scans or CT lumbar spine scans (n = 290).

variations between the follow-up visit and baseline measurements were statistically significant ($P < 0.05$).

Main Results

The results of the logistic regression with the specified 14 variables for clinical response at 4 weeks are presented in Table 5. In the full model, 5 variables were associated with the outcome at $P < 0.1$: obesity, PSPS-2, satisfaction with previous TIDC, radicular compression, and listhesis. The full model was statistically significant, with P equaling 0.02. This model could account for 12% of the variance.

In the simplified model, only the 5 aforementioned variables were retained. Listhesis, radicular compression, and satisfaction with a previous IPMT were positively associated with the positive response, and their ORs were close to 2. However, obesity and PSPS-2 were negatively associated with the outcome, presenting ORs close to 0.5. This model was statistically significant ($P < 0.01$) and could account for 10% of the variance. With a confidence level exceeding 95%, the model exhibited satisfactory goodness of fit (Table 5).

The corresponding ROC curve was plotted, and the AUC was calculated (Fig. 2). The model had an AUC of 0.67 (CI 95%, 0.60-0.74). The models exhibited low sensitivity (9.4% full model, 11.8% simplified model)

Table 5. *Full model and simplified model resulting from logistic regression for clinical response at 4 weeks with specified variables.*

Full model	**B**	**Wald**	***P***	**OR**	**IC95% OR**
Work sick leave	-0.11	0.10	0.75	0.90	(0.47-1.73)
Depression/anxiety	0.02	0.00	0.97	1.02	(0.45-2.29)
Obesity	-0.53	2.99	0.08	0.59	(0.32-1.07)
Existence of another chronic pain condition	-0.29	0.91	0.34	0.75	(0.42-1.35)
PSPS-2	-0.71	3.44	0.06	0.49	(0.23-1.04)
Radicular compression in imaging	0.73	5.81	0.02	2.07	(1.15-3.73)
Herniated disc in imaging	-0.31	1.13	0.29	0.74	(0.42-1.29)
Radiated pain	0.04	0.02	0.90	1.04	(0.59-1.84)
Age > 65 years	0.03	0.01	0.93	1.03	(0.55-1.91)
Chronic therapy with opioid medication	0.31	0.73	0.39	1.36	(0.67-2.73)
Chronic therapy with opioid AND gabapentinoids	-0.48	2.10	0.15	0.62	(0.32-1.19)
Initial ODI ≥ 40	-0.07	0.04	0.84	0.94	(0.49-1.8)
Satisfaction with previous IPMT	0.56	3.42	0.06	1.76	(0.97-3.2)
Listhesis	0.86	6.77	0.01	2.37	(1.24-4.54)
Statistical significance of the model			$P = 0.02$		
Nagelkerke's R Squared			$P = 0.12$		
Hosmer-Lemeshow Test	$\chi^2 = 10.99$	df = 8	$P = 0.20$		
Simplified model (step 10)					
Obesity	-0.53	3.07	0.08	0.59	(0.32-1.07)
PSPS-2	-0.75	4.47	0.03	0.47	(0.24-0.95)
Radicular compression in imaging	0.69	5.87	0.02	2.00	(1.14-3.49)
Satisfaction with previous IPMT	0.54	3.42	0.06	1.72	(0.97-3.06)
Listhesis	0.92	8.72	<0.01	2.50	(1.36-4.6)
Statistical significance of the model	< 0.01				
Nagelkerke's R Squared	0.10				
Hosmer-Lemeshow Test	$\chi^2 = 1.85$	df = 8	$P = 0.99$		

The simplified model was obtained through an automated statistical variable selection method, 'backstep.' ODI: Oswestry Disability Index; TIDC: Interventional Therapy for Chronic Pain; B: coefficient b of the model; Wald: Wald statistical index; *P*: *P*-value; OR: odds ratio; 95% CI OR: 95% confidence interval of the OR; PSPS-2: Persistent Spinal Pain Syndrome Type 2. Calibration was assessed using the Hosmer-Lemeshow test. χ^2: chi-square value; df: degrees of freedom.

but high specificity (97.0% full model, 97.4% simplified model).

The optimism value, derived from bootstrap simulations, was 0.063. The adjusted AUC had a value of 0.602 (CI 95%, 0.53 to 0.67). This finding indicates that the model maintains a moderate capacity to distinguish between classes even after bootstrap validation. The bootstrap shrinkage value was 0.63, suggesting that the model was robust. As for goodness of fit, tests were significant in 3% of cases, indicating that the model was generally well calibrated. The 5 variables included in the simplified model are also those described most frequently in the bootstrap samples (Table 6).

Other Analyses

Two major pathophysiological subgroups were discerned, encompassing 229 out of 319 patients undergoing epidural infiltrations and 74 out of 319 patients receiving therapies targeting the medial branch. Subsequent logistic regression analyses were independently conducted within each subgroup. In the epidural infiltration subgroup, 4 consistent predictors of success emerged. These factors were obesity, listhesis, radicular compression, and PSPS-2, mirroring those identified for the entire cohort. Conversely, the regression within the medial branch therapy subgroup did not unveil any discernible predictor of treatment success. Models in both subgroups showed a satisfactory fit.

A predictive score was developed based on the odds ratios (ORs) of the model variables, as detailed in Table 7. Variables negatively associated with the outcome were reversed., To estimate many points to be assigned to each variable, the OR of each of the variables was divided by the smallest OR. Applying the Hosmer and Lemeshow test to the predictive score yielded a value of 0.92. The AUC of the predictive score was similar to that calculated for the simplified model: 0.66 (95% CI, 0.59-0.72) (Fig. 2).

The metrics of the predictive score according to the cutoff points are presented in Table 8. A summary of the application of the predictive score is available in Table 9.

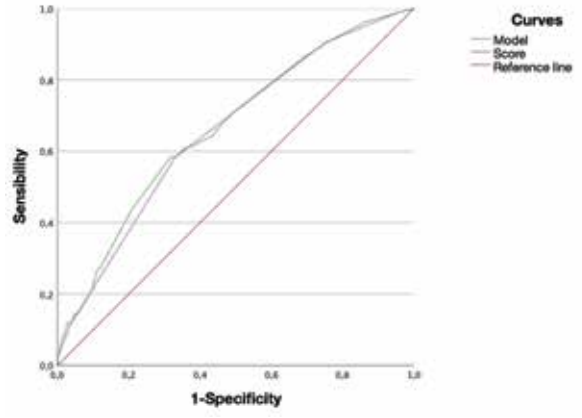

Fig. 2. *ROC curves of the model and the predictive score for the 4-week positive response.*
ROC: Receiver Operating Characteristic Curve

Discussion

Most Significant Results

Patients who were obese or had PSPS-2 were half as likely to respond as patients without these conditions. Factors such as satisfaction with a previous IPMT, radicular compression, or listhesis in imaging were associated with nearly double the probability of obtaining a positive response.

The predictive model comprising these 5 variables demonstrated the capacity to explain a significant, albeit limited, proportion of the observed variability in outcomes. The model's level of discriminative ability is considered adequate in the clinical context. This model is more useful for determining which patients will not benefit from interventional management (especially

Table 6. *Number of occurrences per variable in the bootstrap simulations.*

Variables	n of occurences
Listhesis	74
Radicular compression in imaging	59
PSPS-2	46
Satisfaction with previous IPMT	44
Obesity	42
Chronic therapy with opioid AND gabapentinoids	38
Chronic therapy with opioid medication	16
Herniated disc in imaging	14
Work sick leave	12
Existence of another chronic pain condition	12
Depression/anxiety	8
Initial ODI ≥ 40	8
Age > 65 years	6
Radiated pain	2

The variables included in the simplified model have been highlighted in bold. IPMT: Interventional Pain Management Techniques; PSPS-2: Persistent Spinal Pain Syndrome Type 2; ODI: Oswestry Disability Index.

those undergoing epidural corticosteroid injections) than for identifying those who will. This insight may become a valuable guidance for making informed decisions on whether to advocate or advise against IPMTs for specific CLBP patients.

Limitations

It is crucial to note that the study has a single-center setting by design. While this choice allows for a well-established clinical team to share the experience of managing patients who exhibit predictive factors, the lack of participation of other centers could impact the broader applicability of the findings.

Loss to follow-up is another significant limitation. Factors such as advanced age and the influence of the COVID-19 pandemic may have contributed to these losses. Strategies were implemented to minimize losses, but this aspect should still be considered when interpreting the results of the study. Also, exclusions can introduce biases and affect the representativeness of the sample.

The explanatory capacity of the model is limited, since there is still a significant amount of variability in the data unexplained by the included predictor variables.

The presence of a specific anatomical substrate may condition a more favorable response. However, 70% of the interventions in the study were epidural injections, which may have led the predictive factors of the cohort to gravitate toward the most frequently performed techniques. The subgroup analysis revealed that both listhesis and radicular compression were associated with the response to epidural therapies but not with the response to medial branch therapies. Additionally, 3 other factors that could potentially be common to both groups—obesity, PSPS-2, and satisfaction with previous interventional therapies—were also not associated with the response in the medial branch therapy group. The limited sample size of this subgroup may contribute to the absence of statistically significant associations. Further research with larger sample sizes in this specific subgroup is warranted to validate these findings and explore potential nuances that might influence treatment response.

Interpretation

To the best of our knowledge, there are 17 papers that analyze the association of several factors related to the patients, the patients' pain pathology, imaging findings, or the procedure itself with the outcomes of the IPMTs. Six of these papers are observational prospective studies (22,25,39-42), 9 are observational retrospective studies (43-51), and 2 are sub-studies of clinical trials (52,53). Fifteen studies evaluate factors that predict responses to epidural corticoid infiltrations (25,38-47,50-54), one analyzes pulsed radiofrequency of the dorsal root ganglion (49), and the last includes up to 4 different IPMTs (22).

Patients' satisfaction with previous IPMTs was identified as a predictor for treatment outcomes. Surprisingly, the existing literature often overlooks this

Table 7. *Prediction scores based on the odds ratios of the variables.*

Variable	*P*	OR	CI95%	OR/1.71	Score points
Abscence of obesity	0.08	1.71	(0.94-3.01)	1.00	1
Abscence of PSPS-2	0.03	2.11	(1.06-4.22)	1.23	1
Radicular compression	0.02	2.00	(1.14-3.49)	1.17	1
Satisfaction with previous IPMT	0.06	1.72	(0.97-3.06)	1.01	1
Listhesis	< 0.01	2.50	(1.36-4.6)	1.46	1

OR: odds ratio; 95% CI OR: 95% confidence interval of the OR; PSPS-2: Persistent Spinal Pain Syndrome Type 2; IPMT: Interventional Pain Management Techniques.

Table 8. *Cut-off points for the predictive score.*

Cut-off point	Sensibility (IC95%)	Specificity (IC95%)	PPV (IC95%)	NPV (IC95%)
≥ 1	98.8 (93.5-100)	4.7 (2.4- 8.3)	27.2 (22.3-32.6)	91.7 (61.5-99.8)
≥ 2	90.5 (82.1-95.8)	24.9 (19.5-31)	30.3 (24.7-36.4)	87.9 (77.5-94.6)
≥ 3	58.3 (47.1-69)	67.0 (60.5-73)	38.9 (30.3-48.0)	81.7 (75.4-86.9)
≥ 4	11.9 (5.9-20.8)	96.1 (92.8-98.2)	52.6 (28.9-75.6)	75.2 (69.9-80)
≥ 5	2.4 (0.3- 8.3)	100 (98.4-100)	100 (15.8-100.0)	74 (68.8-78.7)

This table provides details on the sensitivity, specificity, and predictive values at various cut-off points of the score.; PPV: positive predictive value; NPV: negative predictive value; CI95%: 95% confidence interval.

Table 9. *Summary of the application of the predictive score.*

Variable	Points
Abscence of obesity	1
Abscence of PSPS-2	1
Previous satisfaction with IPMT	1
Radicular compression	1
Listhesis	1
Score 0 or 1	The patient is likely not to benefit from intervention.*
Score 2 or greater	The patient could benefit from intervention. Individualized approach recommended.

PSPS-2: Persistent Spinal Pain Syndrome Type 2; IPMT: Interventional Pain Management Technique. *Refers to the response at 4 weeks to the ICDTs performed in the study (caudal or interlaminar corticosteroid epidural injections, pulsed radiofrequency of the dorsal root ganglion, and lumbar medial branch injection or radiofrequency).

factor, despite commonly observing patients who have a history of previous IPMTs.

In a systematic review of the predictive value of imaging findings for responses to lumbar epidural injections, the authors found insufficient evidence to support or refute the role of radicular compression (55). The impact of the degree of radicular compression is also a matter of debate (40,41,43,44,52). The finding of listhesis in imaging is less studied in the literature. Wei et al found no differences in outcomes that could be attributed to whether the radicular compression was caused by listhesis, disc herniation, or canal stenosis (54).

Our findings suggest that patients with PSPS-2 may respond less favorably to IPMTs. More targeted therapies for PSPS-2, such as adhesiolysis or spinal cord stimulation, have not been included in the PRETI-Back study. Therefore, conclusions about the predictive value of PSPS-2 for these other techniques cannot be drawn. The exclusion of patients with a history of lumbar surgery in most studies on predictive factors complicates the understanding of its impact (22,39,42,44,45,47,51-53). Most studies that include patients who have undergone this type of procedure suggest a negative association between previous lumbar surgery and response to epidural infiltrations (25,50,54).

Obesity usually has a negative impact on medical intervention outcomes. However, the evidence regarding its role in IPMTs is inconclusive. Some studies have not found an association (41,49,51,53), while others suggest a relationship (22). Obesity could exert a negative influence on the response to IPMTs due to technical difficulties (46,56) and the condition's association with greater lumbar pathology (57,58) and an unhealthy lifestyle for reasons including lower physical activity.

When considering the management of CLBP, it is essential to bear the patients' employment status in mind. This factor has been shown to be associated with better outcomes after lumbar surgery (59,60). Nevertheless, as was consistent with our findings, other researchers examining this potential predictor observed no association with IPMTs outcomes (22,25,46,53).

Anxiety and depression influence the severity of CLBP and its prognosis and treatment response. However, there is no agreement in the literature regarding the predictive value of these mood disorders, with some authors finding an association with depression (22,54) or anxiety (25) while others find no association (42,53). The negative effect of other chronic pain on interventional outcomes was described in 2 studies (22,49). These findings were not confirmed in our study.

We did not find the presence of disc herniations on imaging to be a standalone predictor of response, a result in line with those recorded by most authors (40,41,46,47,49,50). Two studies, however, indicated the presence of disc herniations as a predictor (25,54). These authors, who selected only patients undergoing epidural infiltrations with radicular pain symptoms and congruent imaging, found better responses in patients who had disc herniations than in those who had spondylolisthesis.

Radiating pain to the lower limb below the knee was not associated with response in our study, an observation consistent with previous findings (25,54).

Our study found no differences between age groups. This factor has been ruled out in most studies (25,39,46,49,51,53,54). Only 2 publications demonstrated an association of age with the response to IPMTs, but these papers showed contradictory results (22,41).

Finally, there is controversy about the impact of the degree of the patient's disability prior to the IPMT on the procedure's outcome, with some authors indicating that patients with higher degrees of disability exhibit better responses (25,46,54) while others describe the opposite (22).

The synthesis of the prediction score had little impact on its discriminatory capacity. The establishment of a cut-off point at 2 points appears to be the most suitable, exhibiting moderate-to-high sensitivity but low specificity. The score is efficient in ruling out patients who will not benefit from intervention, but its main limitation lies in its lower effectiveness in identifying those who may respond favorably. The prediction score

has an easy application in clinical practice and is based on 5 easily obtainable variables (3 clinical parameters and 2 imaging parameters), making it a valuable tool for assessing candidates for IPMTs in cases of CLBP.

Generalizability

Because of the characteristics of the cohort, there are some limitations to its generalizability. All patients included in the study were drawn from a tertiary-center pain clinic. One element that must be considered is the high rate of PSPS-2, 23.2%, which is consistent with 90% of the patients being referred from spinal surgeons. Accordingly, basal measurements of pain intensity and disability yielded rather high scores. The predictive factors appear particularly robust within the population undergoing epidural injections.

Finally, the lack of external validation is a significant limitation for generalizing the results. The need for future research that addresses this aspect should be emphasized to provide greater confidence in the clinical applicability and accuracy of the model. The bootstrap validation has yielded promising results in this regard, offering some reassurance regarding the model's reliability and robustness.

Conclusions

Patients who report satisfaction with previously performed IPMTs for CLBP or who are found to have radicular compression or listhesis in imaging show approximately twice the likelihood of experiencing a positive response 4 weeks after an IPMT as do patients without these characteristics. Patients who are obese or have PSPS-2 exhibit an approximately 50% lower likelihood of short-term response compared to those without these conditions.

Acknowledgements

We would like to acknowledge the contributions of R. Vela Martin, I. Fuertes Arena, L. Velasco Rodrigo, and P. Lejarraga Lavia, for their help with follow-up visits.

We would also like to thank JM Bellón for his assistance with the statistical analysis and modeling.

Authors' Contributions

Santiago Garcia-Hernandez, MD: principal investigator. Main author; Fernando Higuero-Cantonero, MD: principal investigator; Francisco Andrés De la Gala Garcia, MD, PhD: reviewer and investigator. Study designer; Ángel Alonso Chico, MD: reviewer and investigator; Javier Blanco Aceituno, MD: reviewer and investigator. ; Sara Zapatero Garcia, MD, PhD: reviewer and investigator; José Laureano Aguilar Godoy, MD: reviewer and investigator; Javier Hortal Iglesias, MD, PhD: reviewer; Ana Esther Lopez Perez, MD, PhD: Study chair; Ignacio Garutti Martinez, MD, PhD: reviewer and investigator. Data analyzer.

References

1. Veale DJ, Woolf AD, Carr AJ. Chronic musculoskeletal pain and arthritis: Impact, attitudes and perceptions. *Ir Med J* 2008; 101:208-210.
2. Hoy D, Brooks P, Blyth F, Buchbinder R. The epidemiology of low back pain. *Best Pract Res Clin Rheum* 2010; 24:769-781.
3. Hoy D, Bain C, Williams G, et al. A systematic review of the global prevalence of low back pain. *Arthritis Rheum* 2012; 64:2028-2037.
4. Ministerio de Sanidad, Consumo y Bienestar Social, Instituto Nacional de Estadística. *Encuesta Nacional de Salud de España* 2017. Ministerio de Sanidad, Consumo y Bienestar Social, Instituto Nacional de Estadística; 2018. Estado de Salud (Valores porcentuales y medias). Tabla 1.015. www.sanidad.gob.es/estadEstudios/estadisticas/encuestaNacional/encuestaNac2017/encuestaResDetall2017.htm
5. Humbría Mendiola A, Carmona L, Peña Sagredo J, Ortiz A. Impacto poblacional del dolor lumbar en España: Resultados del estudio EPISER. *Revista Española de Reumatología* 2002; 29:471-478.
6. GBD 2017 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990-2017: A systematic analysis for the Global Burden of Disease Study 2017. *Lancet* 2018; 392:1789-1858.
7. Bogduk N. The interbody joint and the intervertebral disc. In: *Clinical Anatomy of the Lumbar Spine and Sacrum*. 4th ed. Elsevier/Churchill Livingstone, 2005, pp 11-28.
8. Amirdelfan K, McRoberts P, Deer TR. The differential diagnosis of low back pain: a primer on the evolving paradigm. *Neuromodulation* 2014; 17:Suppl 2:11-17.
9. Urits I, Burshtein A, Sharma M, et al. Low back pain, a comprehensive review: Pathophysiology, diagnosis, and treatment. *Current Pain Headache Rep* 2019; 23:23.
10. Manchikanti L, Singh V, Pampati V, et al. Evaluation of the relative contributions of various structures in chronic low back pain. *Pain Physician* 2001; 4:308-316.
11. Kreiner DS, Hwang S, Easa J, et al. *Evidence-Based Clinical Guideliens for Multidisciplinary Spine Care: Diagnosis and Treatment of Lumbar Disc Herniation with Radiculopathy*. North American Spine Society; 2012. www.spine.org/Portals/0/assets/downloads/researchclinicalcare/guidelines/lumbardischerniation.pdf
12. Manchikanti L, Falco F, Singh V, et al. An update of comprehensive evidence-

based guidelines for interventional techniques in chronic spinal pain. Part I: Introduction and general considerations. *Pain Physician* 2013; 16:S1-S48.

13. Chou R, Loeser J, Owens D, et al. Interventional therapies, surgery, and interdisciplinary rehabilitation for low back pain: An evidence-based clinical practice guideline from the American Pain Society. *Spine* 2009; 34:1066-1077.
14. National Institute for Health and Care Excellence. *Low back pain and sciatica in over 16s: Assessment and management*. National Institute for Health and Care Excellence; 2016. NICE guideline 59. Updated 12/11/2020. https://www.nice.org.uk/guidance/ng59/resources/low-back-pain-and-sciatica-in-over-16s-assessment-and-management-pdf-1837521693637
15. Manchikanti L, Abdi S, Atluri S, et al. An update of comprehensive evidence-based guidelines for interventional techniques in chronic spinal pain. Part II: Guidance and recommendations. *Pain Physician* 2013; 16:S49-S283.
16. Manchikanti L, Falco F, Pampati V, et al. Cost utility analysis of caudal epidural injections in the treatment of lumbar disc herniation, axial or discogenic low back pain, central spinal stenosis, and post lumbar surgery syndrome. *Pain Physician* 2013; 16:E129-E143.
17. Manchikanti L, Pampati V, Benyamin R, Hirsch J. Cost utility analysis of lumbar interlaminar epidural injections in the treatment of lumbar disc herniation, central spinal stenosis, and axial or discogenic low back pain. *Pain Physician* 2017; 20:219-228.
18. Manchikanti L, Kosanovic R, Pampati V, et al. Equivalent outcomes of lumbar therapeutic facet joint nerve blocks and radiofrequency neurotomy: Comparative evaluation of clinical outcomes and cost utility. *Pain Physician* 2022; 25:179-192.
19. El-Yahchouchi CA, Plastaras CT, Maus TP, et al. Adverse event rates associated with transforaminal and interlaminar epidural steroid injections: A multi-institutional study. *Pain Med* 2016; 17:239-249.
20. Kreiner DS, Matz P, Bono CM, et al. Guideline summary review: An evidence-based clinical guideline for the diagnosis and treatment of low back pain. *Spine J* 2020; 20:998-1024.
21. Koes B, van Tulder M, Thomas S. Diagnosis and treatment of low back pain. *BMJ* 2006; 332:1430-1434.
22. Cohen S, Doshi T, Kurihara C, et al. Multicenter study evaluating factors associated with treatment outcome for low back pain injections. *Reg Anesth Pain Med* 2022; 47:89-99.
23. Carreon LY, Bratcher KR, Ammous F, Glassman SD. Cost-effectiveness of lumbar epidural steroid injections. *Spine* 2018; 43:35-40.
24. Pennington Z, Swanson M, Lubelski D, et al. Comparing the short-term cost-effectiveness of epidural steroid injections and medical management alone for discogenic lumbar radiculopathy. *Clinical Neurol Neurosurg* 2020; 191:105675.
25. Sivaganesan A, Chotai S, Parker S, Asher AL, McGirt MJ, Devin CJ. Predictors of the efficacy of epidural steroid injections for structural lumbar degenerative pathology. *Spine J* 2016; 16:928-834.
26. von Elm E, Altman D, Egger M, Pocock SJ, Gøtzsche PC, Vandenbrouke JP; STROBE Initiative. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: Guidelines for reporting observational studies. *J Clin Epidemiol* 2008; 61:344-349.
27. Garcia-Hernandez S, Higuero-Cantonero F. *Predicting Response to Interventional Pain Management Techniques in Chronic Low Back Pain in a Prospective Cohort*. - Tabular View - ClinicalTrials.gov, (ed 06-15-2020), 2020.
28. Falco FJE, Hirsch JA, Kaye AD, Manchikanti L. *Essentials of Interventional Techniques in Managing Chronic Pain*, Springer Cham, 2018.
29. Manchikanti L, Kaye A, Soin A, et al. Comprehensive evidence-based guidelines for facet joint interventions in the management of chronic spinal pain: American Society of Interventional Pain Physicians (ASIPP) Guidelines Facet Joint Interventions 2020 Guidelines. *Pain Physician* 2020; 23:S1-S27.
30. Manchikanti L, Knezevic N, Navani A, et al. Epidural interventions in the management of chronic spinal pain: American Society of Interventional Pain Physicians (ASIPP) Comprehensive Evidence-Based Guidelines. *Pain Physician* 2021; 24:S27-S208.
31. Williamson A, Hoggart B. Pain: A review of three commonly used pain rating scales. *Journal Clin Nurs* 2005; 14:798-804.
32. Childs J, Piva S, Fritz J. Responsiveness of the numeric pain rating scale in patients with low back pain. *Spine* 2005; 30:1331-1334.
33. Vicente-Herrero MT, Delgado-Bueno S, Bandrés-Moyá F, et al. Valoración del dolor. Revisión comparativa de escalas y cuestionarios. *Rev Soc Esp Dolor* 2018; 25: 228-236.
34. Flórez García M, García Pérez M, García Pérez F, et al. Adaptación transcultural a la población española de la escala de incapacidad por dolor lumbar de Oswestry. *Rehabilitación* 1995; 29:138-145.
35. van Smeden M, Moons K, de Groot J, et al. Sample size for binary logistic prediction models: Beyond events per variable criteria. Stat Methods Med *Res 2019; 28:2455-2474.*
36. Ogundimu E, Altman D, Collins G. Adequate sample size for developing prediction models is not simply related to events per variable. *J Clin Epidemiol* 2016; 76:175-182.
37. Peduzzi P, Concato J, Kemper E, Holford TR, Feinstein AR. A simulation study of the number of events per variable in logistic regression analysis. *J Clin Epidemiol* 1996; 49:1373-1379.
38. Harrell F, Lee K, Califf R, et al. Regression modelling strategies for improved prognostic prediction. *Stat Med* 1984; 3:143-152.
39. Cyteval C, Fescquet N, Thomas E, et al. Predictive factors of efficacy of periradicular corticosteroid injections for lumbar radiculopathy. *AJNR Am J Neuroradiol* 2006; 27:978-992.
40. Lechmann M, Rosskopf A, Ehrmann C, Sutter R, Pfirrmann CWA, Peterson CK. Relationship of specific MRI findings to treatment outcomes in patients receiving transforaminal epidural steroid injections. *Skeletal Radiol* 2016; 45:1677-1685.
41. Ekedahl H, Jönsson B, Annertz M, Frobell RB. The 1-year results of lumbar transforaminal epidural steroid injection in patients with chronic unilateral radicular pain: The relation to MRI findings and clinical features. *Am J Phys Med Rehabil* 2017; 96:654-662.
42. Jindal R, Rudol G, Okafor B, Rambani R. Role of psychological distress screening in predicting the outcomes of epidural steroid injection in chronic low back pain. *J Clin Orthop Trauma* 2021; 19:26-33.
43. Choi S, Song J, Kim C, et al. The use of magnetic resonance imaging to predict the clinical outcome of non-surgical treatment for lumbar intervertebral disc herniation. *Korean J Radiol* 2007;

8:156-163.

44. Paidin M, Hansen P, McFadden M, Kendall R. Contrast dispersal patterns as a predictor of clinical outcome with transforaminal epidural steroid injection for lumbar radiculopathy. *PM R* 2011; 3:1022-1027.
45. Lee JW, Choi SW, Park SH, Lee GY, Kang HS. MR-based outcome predictors of lumbar transforaminal epidural steroid injection for lumbar radiculopathy caused by herniated intervertebral disc. *Eur Radiol* 2013; 23:205-211.
46. McCormick Z, Cushman D, Casey E, Garvan C, Kennedy DJ, Plastaras C. Factors associated with pain reduction after transforaminal epidural steroid injection for lumbosacral radicular pain. *Arch Phys Med Rehabil* 2014; 95:2350-2356.
47. Tecer D, Adiguzel E, Tan A, Taskaynatan M. Role of magnetic resonance imaging in ascertaining the success of transforaminal epidural steroid injection for lumbar radicular pain. *Pain Med* 2017; 18:645-650.
48. Williams C, Maher C, Latimer J, et al. PACE--the first placebo controlled trial of paracetamol for acute low back pain: statistical analysis plan. *Trials* 2013; 14:248.
49. Kim S, Park S, Yoon D, Yoon KB, Kim Sh. Predictors of the analgesic efficacy of pulsed radiofrequency treatment in patients with chronic lumbosacral radicular pain: A retrospective observational study. *J Pain Res* 2018; 11:1223-1230.
50. Park D, Kang S, Park J. Factors predicting favorable short-term response to transforaminal epidural steroid injections for lumbosacral radiculopathy. *Medicina* 2019; 55:162.
51. Şencan S, Çelenlioğlu A, Asadov R, Gündüz O. Predictive factors for treatment success of transforaminal epidural steroid injection in lumbar disc herniation-induced sciatica. *Turk J Med Sci* 2020; 50:126-131.
52. Ghahreman A, Bogduk N. Predictors of a favorable response to transforaminal injection of steroids in patients with lumbar radicular pain due to disc herniation. *Pain Med* 2011; 12:871-879.
53. Turner J, Comstock B, Standaert C, et al. Can patient characteristics predict benefit from epidural corticosteroid injections for lumbar spinal stenosis symptoms? *Spine J* 2015; 15:2319-2331.
54. Wei J, Chotai S, Sivaganesan A, et al. Effect of pre-injection opioid use on post-injection patient-reported outcomes following epidural steroid injections for radicular pain. *Spine J* 2018; 18:788-796.
55. Benny B, Patel M. Predicting epidural steroid injections with laboratory markers and imaging techniques. Spine J 2014; 14:2500-2508.
56. Kula A, Riess M, Ellinas E. Increasing body mass index predicts increasing difficulty, failure rate, and time to discovery of failure of epidural anesthesia in laboring patients. *J Clin Anesth* 2017; 37:154-158.
57. Xu X, Li X, Wu W. Association between overweight or obesity and lumbar disk diseases: A meta-analysis. *J Spinal Discord Tech* 2015; 28:370-376.
58. Pinto E, Teixeria A, Frada R, et al. Patient-related risk factors for the development of lumbar spine adjacent segment pathology. *Orthop Rev* 2021; 13:24915.
59. Chan A, Bisson E, Bydon M, et al. Predictors of the best outcomes following minimally invasive surgery for grade 1 degenerative lumbar spondylolisthesis. *Neurosurgery* 2020; 87:1130-1138.
60. Anderson P, Schwaegler P, Cizek D, Leverson G. Work status as a predictor of surgical outcome of discogenic low back pain. *Spine* 2006; 31:2510-2515.