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Relationship between Time Elapsed Since Pain Onset and Efficacy of Pain Relief in Patients Undergoing Lumbar Percutaneous Epidural Adhesiolysis

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Purpose: The aim of this study was to investigate the relationship between pain duration and pain relief after epidural adhesiolysis.
Materials and Methods: Patients with low back pain who underwent lumbar epidural adhesiolysis were enrolled. A clinically significant reduction in pain score was defined as a ≥30% reduction at 6-month follow-up evaluation. Variables were compared based on pain duration categories. Changes in pain scores and pain outcome were also compared. Logistic regression analysis was conducted to identify factors associated with pain relief after adhesiolysis.
Results: A total of 169 patients, including 77 (45.6%) patients with a favorable pain outcome, were included for analysis. Patients with a pain duration ≥3 years reported lower baseline pain scores and showed more frequent severe central stenosis. Pain scores significantly decreased over time after the procedure except in patients with a pain duration ≥3 years. Most patients who experienced pain for ≥3 years showed poor pain relief (80.8%), unlike other pain duration categories (pain duration <3 months=48.1%, 3 months–1 year=51.8%, 1–3 years=48.6%). A pain duration ≥3 years and lower baseline pain score were independent factors associated with an unfavorable pain outcome.
Conclusion: Pain lasting ≥3 years prior to lumbar epidural adhesiolysis was associated with worse outcomes in terms of pain relief. Therefore, this intervention should be considered early before pain chronification in patients with low back pain.

Key Words: Analgesia, chronic pain, low back pain, pain management, spine

INTRODUCTION

Most people experience some form of low back pain at least once in their lives, and low back pain is a common cause of disability.[1,2] High socioeconomic costs are incurred in the management of chronic low back pain.[3] To alleviate pain, various conservative treatments, such as manual manipulation, physical therapy, analgesic medication, or epidural steroid injections, are performed.[4-6] Percutaneous epidural adhesiolysis may be considered as a non-surgical therapeutic option for patients who do not respond to conventional treatments.[7-10]

Percutaneous epidural adhesiolysis, also known as percutaneous epidural neuroplasty, was first introduced in the late 1980s as a minimally invasive procedure.[7,8] The original concept of this procedure included disruption of perineural fibrosis and inhibition of repeated scar formation on affected spinal levels.[7,8,11] Because this interventional procedure has a higher cost burden than a single epidural steroid injection, most patients expect the analgesic benefit will last longer.[12] Therefore, clinical information regarding factors associated with long-term pain relief after this procedure is important for decision-making involving patients and clinicians.

Patients with longer pain durations are generally considered likely to experience a poor response to most treatment approaches for chronic low back pain.[13] Central sensitization to pain might be established in patients with pain for many years.[14] Furthermore, patients with longer durations of low

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back pain might suffer from comorbid mental health problems or sleep disorders.[15] Poor functional ability resulting from pain is also frequently observed in this population.[16] Therefore, we hypothesized that a longer period of time from pain onset would be associated with poorer pain relief of lumbar percutaneous epidural adhesiolysis.

The purpose of this retrospective observational study was to investigate the relationship between time elapsed since pain onset and efficacy of pain relief in patients undergoing percutaneous epidural adhesiolysis. In addition, pain duration was evaluated as an independent factor associated with analgesic efficacy.

MATERIALS AND METHODS

Study population

This study was approved by the appropriate Institutional Review Board, and informed consent was not required because of the retrospective nature (No. 4-2023-0030). This manuscript adheres to the applicable STROBE checklists for observational studies. Adult patients with a diagnosis of lumbar spinal disease confirmed based on imaging studies, who underwent percutaneous epidural adhesiolysis for treatment of low back or low extremity pain in our clinic from 2012 to 2021, and who were followed for at least 6 months were enrolled in the study. Exclusion criteria included no pain score measurement at four specific assessment times (baseline before procedure and 1, 3, and 6 months after procedure), incomplete medical records or procedure notes, and patients lacking fluoroscopic images obtained during the procedure.

Fluoroscopy-guided lumbar percutaneous epidural adhesiolysis

All procedures were performed according to standard protocols by two practitioners with similar clinical experience. The procedure was performed under fluoroscopic guidance (ARCADIS Varic 2013; Siemens Medical Solutions, Erlangen, Germany) in a sterile operating room with monitoring equipment. The patients were positioned prone, and the lower back was draped in a sterile fashion. The sacral hiatus was confirmed by an abrupt drop off from the caudal end of the S4 lamina in the lateral view. After confirming the needle inlet point, local anesthesia was administered. A 10-gauge guide Tuohy needle was advanced into the sacral canal via the sacral hiatus, and the epidural space was ensured by injecting 2–3 mL of contrast media. After confirming correct needle placement, a steerable navigation catheter (ST. Reed plus®, Seawon Meditech, Bucheon, Republic of Korea) was gently inserted through a guide needle toward the target site under fluoroscopy. At the target site, 2–3 mL of the contrast medium was injected to verify catheter placement in the epidural space and medium spread to the desired target area but not into the dura mater or intravascular site. After confirming correct epidural flow, 10 mL of 1% lidocaine mixed with a typical dose of 5 mg of dexamethasone and 1500 IU hyaluronidase was slowly injected at each target site for adhesiolysis. After postoperative recovery, the patient was discharged when all measured parameters were satisfactory. The first follow-up visit was scheduled at 4 weeks after the procedure for all patients.

Patient demographics and clinical data measurements

Patient demographics, pain-related factors, and clinical data were collected from electronic medical record chart review. Patient characteristics included age, sex, body mass index (BMI), medications for diagnosed comorbidities (cardiovascular disease, diabetes mellitus), and lumbar surgery history. The time elapsed since onset of the current pain episode (pain duration), baseline pain score defined as average pain intensity on a numeric rating scale (NRS, 0–10) during the past 4 weeks, opioid usage ≥1 month before adhesiolysis, and presence of neurogenic intermittent claudication symptoms or lumbosacral radiculopathy (sciatica) were considered as pain-related factors. Patients were divided into four categories of pain duration (time since current pain onset): <3 months, ≥3 months and <1 year, ≥1 year and <3 years, and ≥3 years. Patients with <4 weeks of pain were typically asked to rate their average pain intensity during the past 24 hours. Oxycodone, hydromorphone, tramadol, codeine, fentanyl patch, and buprenorphine patch were administered as opioid medications. Based on MRI results with final reports by an independent radiologist, presence of herniated disc, central or foraminal stenosis with grading,[17,18] compression fracture, and spondylolisthesis were analyzed. Pain scores were measured at 1, 3, and 6 months after the procedure. For this study, a favorable pain outcome was defined as a ≥30% decrease in pain score, which is regarded as a clinically meaningful change in pain intensity on a 0–10 NRS,[19] at 6 months after adhesiolysis without an increase in analgesic medication.

Statistical analysis

Descriptive data are presented as means±standard deviations (SD) for continuous variables and as numbers (percentages) for categorical variables. The normality of the distribution was assessed using the Shapiro–Wilk test. Patient demographics, pain-related data, and MRI findings based on pain duration category were compared using one-way analysis of variance with Bonferroni post- hoc test or Kruskal–Wallis test for continuous variables and chi-squared test followed by within-group comparisons using post-hoc pairwise comparisons with Bonferroni corrections for categorical variables. Comparison of NRS pain scores between pain duration categories at each assessment time point after the procedure and changes between assessment time points within a group were compared using linear mixed model. The trend in the percentage of patients with poor analgesia at 6 months after the procedure based on

pain duration category was analyzed using the chi-square test for linear by linear association. Variables, such as age, degree of central stenosis, and pain duration, potentially can violate collinearity, thus, multicollinearity in the regression model was tested using variance inflation factors (VIF). A multivariable logistic regression model, with backward elimination, was constructed to identify factors associated with poor analgesia at 6 months after the procedure, and adjusted odds ratios (aOR) and 95% confidence intervals (CI) were calculated. All statistical analyses were performed using the Statistical Package for the Social Sciences, version 26.0 (IBM Corp, Armonk, NY, USA). Bonferroni-adjusted *p*-values<0.05 were considered statistically significant.

RESULTS

A total of 169 patients between the ages of 24 and 91 years were included for analysis, comprising 77 patients (45.6%) who reported clinically meaningful pain relief (≥30% pain reduction at the 6-month follow-up) and 92 patients (54.4%) who reported poor pain relief after adhesiolysis. The numbers of patients with a pain duration of <3 months, 3 months–1 year, 1–3 years, and ≥3 years were 52 (30.8%), 56 (33.1%), 35 (20.7%), and 26 (15.4%), respectively (Fig. 1).

Patient demographics, pain-related data, and pre-procedural MRI findings were compared between pain duration categories (Table 1). Age, sex, and BMI were similar regardless of pain duration. In addition, a significant difference was not found in the percentages of patients with previous lumbar surgery history and the prevalences of medical comorbidities between pain duration categories. The prevalence of neurogenic intermittent claudication symptoms and radicular pain and opioid usage were comparable among pain duration categories. However, patients with pain duration ≥3 years reported lower pain scores before the procedure than did patients with pain duration <3 months (6.0±1.5 vs. 7.0±1.6; adjusted p=0.048). Although there was a difference in baseline pain scores prior to the procedure, no significant difference was found between patients with pain duration ≥3 years and the other two groups (3 months–1 year group=7.0±1.8, adjusted p=0.065; 1–3 years group=7.1±1.6, adjusted p=0.073). In pre-procedural MRI findings, moderate-to-severe lumbar central stenosis was frequently observed in patients with pain duration ≥3 years, compared with patients with a pain duration of 1–3 years (57.7% vs. 22.9%; adjusted p=0.048). Although moderate-to-severe lumbar central stenosis was observed frequently in the pain duration ≥3 years group, there were no significant differences in the proportion of patients between the pain duration ≥3 years group and the other two groups (<3 months group=34.6%, adjusted p=0.528; 3 months–1 year group=33.9%, adjusted p=0.330). Other lumbar pathology findings on MRI were comparable between pain duration groups.

Changes in patient-reported pain scores throughout the assessment times based on pain duration category are shown in Fig. 2. Baseline pain scores before the procedure were significantly lower in patients experiencing pain for ≥3 years than in subjects reporting pain duration <3 years (p=0.033). Significant

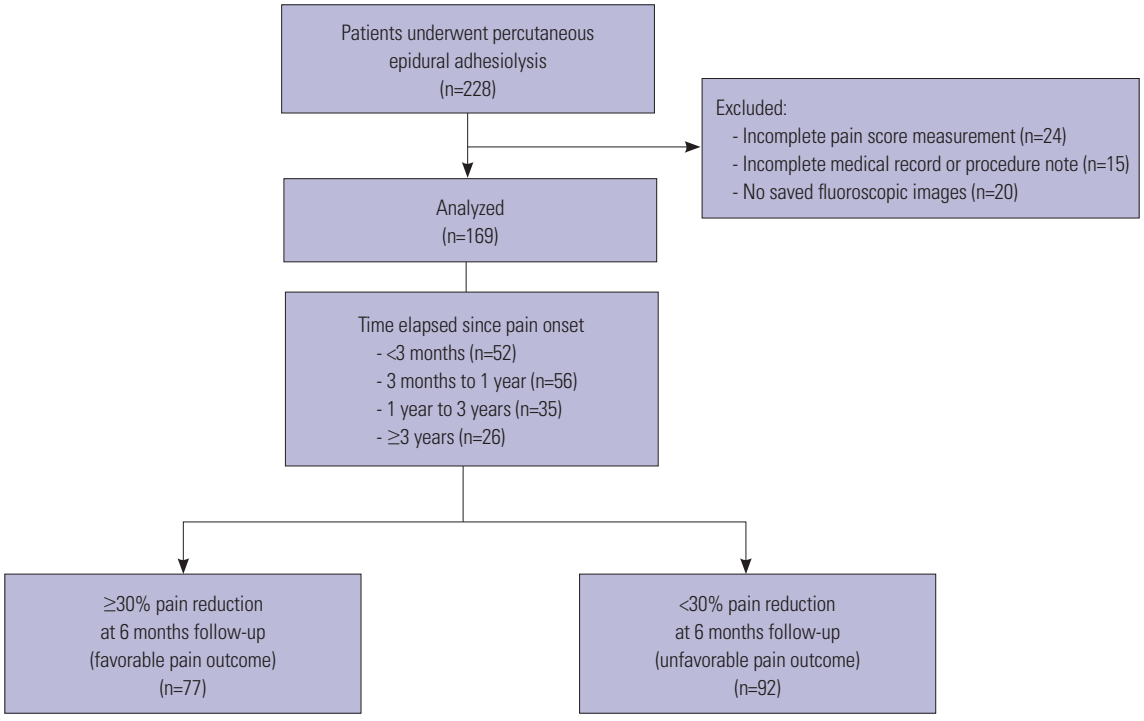

Fig. 1. Flow chart of the study.

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Table 1. Comparison of Patient Characteristics, Clinical Data, and Pre-Procedural Mri Findings Based on Pain Duration Category among Patients Who Received Percutaneous Epidural Adhesiolysis

	Time elapsed since pain onset (Pain duration)				*p* value
	<3 months (n=52)	3 months–1 year (n=56)	1–3 years (n=35)	≥3 years (n=26)	
Patient characteristics					
Age, yr	65.1±12.0 (39–91)	67.2±12.1 (24–89)	66.7±11.9 (40–83)	68.1±6.3 (54–87)	0.673
Female, sex	30 (57.7)	36 (64.3)	14 (40.0)	12 (46.2)	0.108
BMI, kg/m^2	24.7 (21.9–26.6)	24.3 (23.1–26.7)	24.3 (23.4–26.7)	24.6 (23.5–26.5)	0.936
Lumbar surgery history	9 (17.3)	5 (8.9)	11 (31.4)	6 (23.1)	0.052
Medical comorbidities					
Cardiovascular disease	27 (51.9)	39 (69.6)	24 (68.6)	19 (73.1)	0.149
Diabetes mellitus	14 (26.9)	15 (26.8)	10 (28.6)	4 (15.4)	0.641
Pain-related data					
Baseline pain score, 0–10 NRS	7.0±1.6 (4.0–10.0)[§]	7.0±1.8 (4.0–10.0)	7.1±1.6 (4.0–10.0)	6.0±1.5 (4.0–10.0)*	0.033
Opioid usage	41 (78.8)	41 (73.2)	26 (74.3)	18 (69.2)	0.814
Lumbosacral radiculopathy	49 (94.2)	55 (98.2)	34 (97.1)	22 (84.6)	0.070
Neurogenic claudication	22 (42.3)	28 (50.0)	18 (51.4)	17 (65.4)	0.294
Pre-procedural MRI findings					
Herniated disc	46 (88.5)	54 (96.4)	29 (82.9)	25 (96.2)	0.103
Moderate-to-severe central stenosis	18 (34.6)	19 (33.9)	8 (22.9)[§]	15 (57.7)[‡]	0.044
Moderate-to-severe foraminal stenosis	16 (30.8)	26 (46.4)	17 (48.6)	13 (50.0)	0.221
Compression fracture	7 (13.5)	7 (12.5)	2 (5.7)	1 (3.8)	0.412
Spondylolisthesis	7 (13.5)	11 (19.6)	7 (20.0)	3 (11.5)	0.678

BMI, body mass index; NRS, numeric rating scale.
Values are presented as a mean±standard deviation (range), median (interquartile range), or number of patients (%).
The results of post-hoc testing with Bonferroni-corrected p<0.05 are indicated as: *vs. <3 months group; [†]vs. 3 months–1 year group; [‡]vs. 1–3 years group; [§]vs. ≥3 years group.

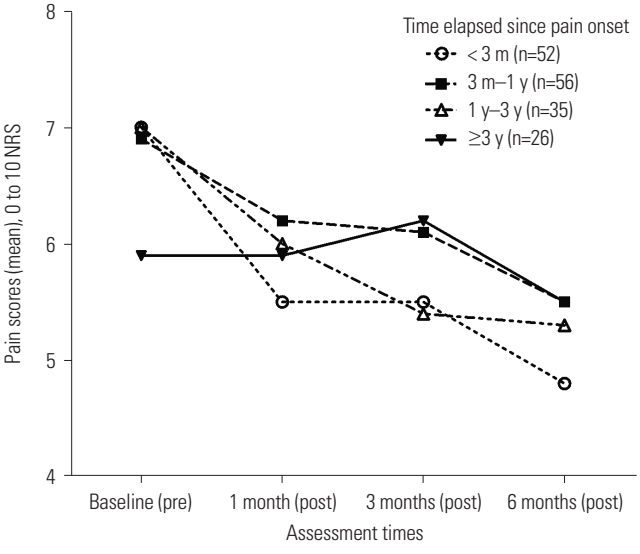

Fig. 2. Changes in mean pain scores based on the numeric rating scale (NRS) after percutaneous epidural adhesiolysis according to pain duration category at each assessment point.

differences were not found in post-procedural pain scores between pain duration category groups at 1-, 3-, and 6-month assessments (p=0.358, p=0.555, and p=0.181, respectively). In patient groups with pain durations of <3 months, 3 months–1 year, and 1–3 years, pain scores at all follow-up times were lower than those at baseline, indicating significant decreases over time after the procedure (F=37.920, p<0.001, F=39.784, p<0.001, and F=36.927, p<0.001, respectively). However, in the patient group with a pain duration ≥3 years, significant differences were not observed in changes from baseline in pain scores at any follow-up time (F=2.098, p=0.152). The interaction of patient groups based on pain duration category by assessment time in pain scores was significant (p Group x Time=0.003).

Significant differences were observed in pain outcomes after the procedure among pain duration categories (p=0.033). The proportion of patients who reported poor pain relief at 6 months after the procedure was highest in the pain duration ≥3 years group (21 of 26 patients, 80.8%), and a significant difference was found in comparison with pain duration <3 months groups (48.1%, adjusted p=0.042). Although there was a difference in the proportion of patients reporting poor pain relief following a procedure over a 6 month period, this difference was not statistically significant between the pain duration ≥3 years and the other two groups (3 months–1 year group=51.8%, adjusted p=0.090; 1–3 years group=48.6%, adjusted p=0.096). Except for the pain duration ≥3 years group, no significant difference was found in pain outcomes among the <3 months group, 3 months–1 year group, and 1–3 years group (all adjustedp >0.999) (Fig. 3).

There were no high intercorrelations among independent

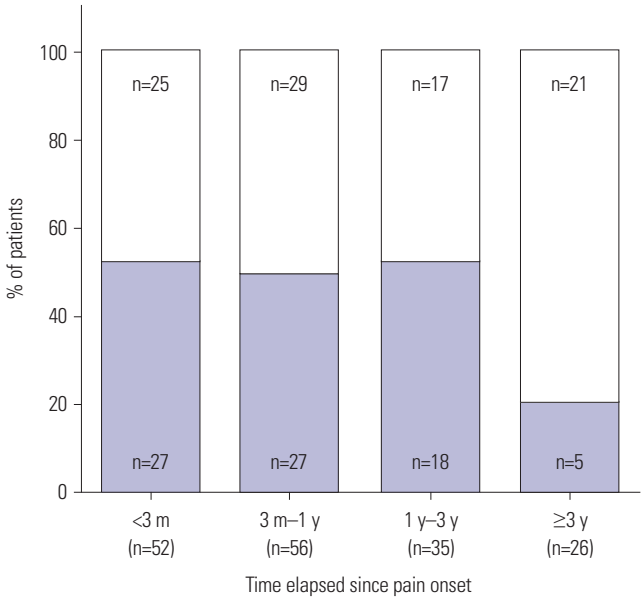

Fig. 3. The percentages of patients with favorable (■, ≥30% pain reduction) and unfavorable (□, <30% pain reduction) pain outcomes at 6 months after percutaneous epidural adhesiolysis in each pain duration category.

variables (VIF of age=1.418, VIF of central stenosis=1.109, VIF of pain duration=1.057). The results of logistic regression analyses to identify factors associated with unfavorable pain outcomes (<30% pain reduction) at 6 months after percutaneous epidural adhesiolysis are shown in Table 2. Multivariable logistic regression analysis revealed that pain duration ≥3 years (aOR=4.379, 95% CI=1.365–14.050, p=0.013) and lower baseline pain score (aOR=0.743, 95% CI=0.606–0.910, p=0.004) were independent factors associated with unfavorable pain outcomes at 6 months after percutaneous epidural adhesiolysis.

DISCUSSION

Although different cut-offs for pain duration from 3 to 12 months were used in previous reports, longer pain duration was consistently associated with poor outcomes in terms of pain relief or functional improvement after lumbar surgery.[20-24] Only a few studies have been conducted on the relationship between pain duration prior to surgery and analgesic efficacy of non-surgical pain interventional procedures in patients with low back pain. In a previous study, a negative correlation was

Table 2. Factors Associated with an Unfavorable Pain Outcome (<30% Pain Reduction) at 6 Months after Percutaneous Epidural Adhesiolysis: Results from Logistic Regression Analyses

Variables	Crude OR	95% CI	*p* value	Adjusted OR	95% CI	*p* value
Patient characteristics						
Age, yr	0.984	0.945–1.025	0.442			
Female, sex	1.502	0.742–3.041	0.259			
BMI, kg/m^2	0.999	0.891–1.120	0.989			
Lumbar surgery history, yes	0.828	0.335–2.046	0.682			
Medical comorbidities, yes						
Cardiovascular disease	1.556	0.611–3.963	0.354			
Diabetes mellitus	0.948	0.416–2.160	0.899			
Pain-related data						
Pain duration						
<3 months	1.000					
3 months–1 year	1.168	0.501–2.722	0.720	1.178	0.529–2.621	0.688
1–3 years	1.196	0.457–3.130	0.716	1.098	0.445–2.712	0.839
≥3 years	4.191	1.210–14.514	0.024	4.379	1.365–14.050	0.013
Baseline pain score, NRS	0.739	0.598–0.913	0.005	0.743	0.606–0.910	0.004
Opioid usage, yes	1.481	0.659–3.325	0.341			
Lumbosacral radiculopathy, yes	0.770	0.157–3.772	0.747			
Neurogenic claudication, yes	1.341	0.656–2.741	0.421			
Pre-procedural MRI findings						
Herniated disc, yes	0.595	0.172–2.055	0.411			
Moderate-to-severe central stenosis, yes	1.322	0.610–2.862	0.479			
Moderate-to-severe foraminal stenosis, yes	0.927	0.437–1.969	0.844			
Compression fracture, yes	2.814	0.795–9.963	0.109	2.676	0.853–8.394	0.091
Spondylolisthesis, yes	2.455	0.938–6.426	0.067	2.508	0.995–6.320	0.051

OR, odds ratio; CI, confidence interval; BMI, body mass index; NRS, numeric rating scale.

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reported between the duration of pain before injection and duration of analgesic effect after injection in patients who received transforaminal epidural injection.[25] In this study, when pain duration ≥3 years was used as a cut-off, the group with a pain duration ≥3 years exhibited poor pain relief after percutaneous epidural adhesiolysis. Furthermore, pain lasting ≥3 years was an independent factor associated with an unfavorable outcome in terms of pain relief after the procedure.

In the current study, patients experiencing pain ≥3 years had higher graded lumbar central stenosis on MRI, which may indicate some technical difficulties during the procedure. However, lumbar spine pathologies confirmed on pre-procedural MRI, including severe central stenosis, were not considered significant factors associated with pain outcomes following percutaneous epidural adhesiolysis in our results. In the present study, lower baseline pain score and pain duration ≥3 years were independent factors associated with pain outcome. Notably, patients with pain lasting ≥3 years mostly reported moderate pain intensity before the procedure, as represented by lower pain score, and patients with pain lasting <3 years mostly reported severe pain intensity. In addition, most patients experiencing pain ≥3 years reported similar pain scores that did not markedly change after the procedure. These results indicate that pain becomes fixed and treatment-resistant due to chronification caused by various intrinsic and extrinsic factors.[26,27] Therefore, pain management for this population is challenging, and integrated personalized strategies based on biological, psychological, physiological, and socio-economical states are needed.[27,28]

Chronic pain is currently defined as persistent or recurrent pain that lasts longer than 3 months.[29] This definition based on a temporal criterion appears to be clear and operationalized; however, pain chronicity is a complicated process involving factors other than just pain and continues for a long time. To evaluate the stage of chronicity in low back pain, a comprehensive approach including pain intensity and frequency, multisite pain, analgesic use, and health care utilization patterns have been proposed.[30] Furthermore, psychological and functional states of patients are considered important factors in assessing the chronicity of low back pain.[31] In the present study, patient groups with pain duration between 3 months and 3 years showed similar pain outcomes, compared with the group with a pain duration <3 months, which could be classified as acute pain. Patient groups with a pain duration between 3 months and 3 years, with chronic pain based on the current definition, showed better pain relief than patients experiencing pain ≥3 years. Although a cut-off of ≥3 years of pain cannot be generalized in all clinical settings, our results indicate that percutaneous epidural adhesiolysis may provide better efficacy of pain relief to select patients, even those suffering from pain >3 months, when this intervention is offered earlier before pain becomes a chronic debilitating condition that may be refractory to therapies.

The present study has several limitations. This retrospective study was conducted in a single center with a relatively small cohort involving a homogeneous ethic population. Other than pain scores, treatment outcome measures after adhesiolysis for assessment of functional status, quality of life, and employment status were not investigated. Most patients were already using pain medications or had received some injection therapies at their initial visit to our pain clinic in a university hospital. This potential confounder could not be controlled and might have affected the results of this study. Although patients with fluoroscopic image data from the procedure were included, detailed contrast dispersion patterns were not analyzed. In addition, a real world clinical practice model was used in which the attending physician in charge determined the timing of the procedure, and other treatments, such as physical rehabilitation therapy, could not be excluded during follow-up.

In conclusion, the results of this study indicate that patients who experience low back pain for ≥3 years do not obtain as good a clinical outcome in terms of pain relief as patients who experience pain for <3 years prior to percutaneous epidural adhesiolysis. Most patients experiencing pain ≥3 years reported unchanged or similar pain scores after the procedure. Therefore, this intervention should be considered early for select patients with low back pain to improve its analgesic efficacy before pain becomes fixed.

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