KJP

Korean J Pain 2023;36(2):184-194
https://doi.org/10.3344/kjp.22289
pISSN 2005-9159, eISSN 2093-0569

Clinical Research Article

Effectiveness of percutaneous epidural neuroplasty using a balloon catheter in patients with chronic spinal stenosis accompanying mild spondylolisthesis: a longitudinal cohort study

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ABSTRACT

Background: Degenerative lumbar spondylolisthesis (DLS) is frequently associated with lumbar spinal stenosis (LSS) and conservative treatments such as epidural steroid injection do not have long-term benefits in LSS patients with DLS. This study evaluated the effectiveness of percutaneous epidural neuroplasty using a balloon catheter in patients with LSS and DLS.
Methods: Patients' sex, age, body mass index, diabetes, hypertension, stenosis grading, pain duration, location, pain intensity, and medications were retrieved from electronic medical records. At 1, 3, and 6 months following the procedure, data on pain severity, medication usage, and physical functional status were analyzed. A generalized estimating equations model was used at the six-month follow-up. Patients were divided into those with DLS (the spondylolisthesis group) and those without DLS (the no spondylolisthesis group) to evaluate whether the effects of percutaneous epidural neuroplasty using a balloon catheter were different.
Results: A total of 826 patients were included (spondylolisthesis: 433 patients, 52.4%; no spondylolisthesis: 393 patients, 47.6%). Age, body mass index, hypertension, pain location, and stenosis grading were statistically different between the two groups. The generalized estimating equations analyses with unadjusted and adjusted estimation revealed a significant improvement in the estimated mean numerical rating scale of pain intensities compared to that at baseline in both groups ($P < 0.001$). Any adverse events that occurred were minor and temporary.
Conclusions: Percutaneous epidural neuroplasty using a balloon catheter may be an alternative treatment option for patients with chronic LSS, regardless of accompanying DLS, who have had failed conservative management.

Keywords: Chronic Pain; Injections, Epidural; Low Back Pain; Lumbar Vertebrae; Neuroplasty; Pain Management; Spinal Stenosis; Spondylolisthesis.

Received August 17, 2022; Revised October 12, 2022; Accepted October 13, 2022

Handling Editor: Young Hoon Kim

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Previous presentation at conferences: This work was presented in the 72th Scientific Meeting of the Korean Pain Society held in Seoul, Korea (2022).

INTRODUCTION

Degenerative lumbar spondylolisthesis (DLS), which is accompanied by degenerative alterations without a disruption or defect in the vertebral ring, is the term used to describe the acquired displacement of a vertebra over the next vertebra [1]. DLS is frequently associated with spinal stenosis [2,3]. DLS may be asymptomatic or may present as low back pain, leg pain, neurogenic claudication, altered gait, cold feet, and unpredictable falling during walking [3]. DLS symptoms are currently managed by non-surgical treatment methods, such as anti-inflammatory drugs, opioids, weight control, management of osteoporosis, physical therapy, and epidural steroid injection (ESI), which have been around for over 15 years [3–5]. In order to treat neurogenic claudication, back pain, and radicular pain, ESI with a local anesthetic is administered across the DLS region [6]. However, long-term follow-up studies of patients undergoing ESI revealed only significant short-term improvements and no long-term benefits [7].

Regarding lumbar spinal stenosis (LSS) with symptoms similar to DLS, there is scientific proof that percutaneous epidural adhesiolysis with a Racz-type catheter, also known as percutaneous epidural neuroplasty, is more efficient than traditional ESI for managing lumbar radiculopathy [8–10]. However, its long-term effects still remain uncertain and controversial. A recent randomized controlled trial revealed that percutaneous epidural neuroplasty was more effective with a balloon catheter than with a Racz catheter [11]. In previous studies, the authors demonstrated that percutaneous epidural neuroplasty with a newly created inflatable balloon catheter (ZiNeu®; JUVENUI, Seoul, Korea) may effectively treat patients with severe adhesions or stenosis while overcoming the drawbacks of earlier balloon-less neuroplasty catheters [11–15]. Although DLS is known to be associated with unsuccessful outcomes in percutaneous epidural neuroplasty [16], there are no studies to date on the effectiveness of percutaneous epidural neuroplasty using a balloon catheter in patients with chronic LSS accompanying DLS.

Therefore, in this longitudinal, cohort study, the effectiveness of percutaneous epidural neuroplasty using a balloon catheter was assessed in patients with chronic LSS accompanying DLS with the purpose of helping patients select the procedure and predict its postoperative outcomes.

MATERIALS AND METHODS

1. Study design and participants

This study was conducted retrospectively at the pain clinic in the Asan Medical Center. All data used in this study were itemized and filled out in the patients' electronic medical records when the patient visited the pain clinic. The Institutional Review Board (IRB number, 2019-1612) approved this retrospective study and waived the requirement for obtaining informed consent because only documented data were reviewed.

Patients who had undergone percutaneous epidural neuroplasty using a ZiNeu® catheter between 2014 and 2018 were included. The following were the criteria for inclusion: (1) patients aged 50 to 90 with radicular leg pain and either back pain or persistent (≥ 3 months) LSS; (2) ≥ 6 on the 11-point numerical rating scale (NRS), where 0 is no pain and 10 is the most severe pain; (3) prior ineffectiveness of conservative care, such as physical therapy, exercise therapy, or analgesic drugs; (4) validation of the type and severity of spinal stenosis by magnetic resonance imaging (MRI); and (5) no long-term (*i.e.*, more than a month) effect of typical interventional methods, including interlaminar, transforaminal, caudal ESI, or even percutaneous epidural neuroplasty using a balloonless catheter (minimum pain reduction response, 50%) (Racz® or NaviCath®).

The following were the exclusion criteria: (1) history of prior lumbar spine surgery, (2) failure to perform the procedure properly due to dura puncture or severe adhesion, (3) failure to rule out vascular disease or a condition with other origins, such as the lumbar facet joint, (4) grade 3, 4, or unstable DLS, (5) allergies to steroids or contrast dyes, (6) coagulation disorder, (7) unstable or uncontrollable opioid use, (8) lactation or pregnancy, (9) injection site or systemic infection, (10) cancer, and (11) unstable psychiatric or medical condition.

2. Percutaneous epidural neuroplasty using a balloon catheter

In a recent article, the authors discussed how to use an inflatable balloon catheter for percutaneous epidural adhesiolysis and decompression [11,13–15,17]. After sterile preparation, 1% lidocaine was injected into the skin and soft tissue. A 10-gauge guide needle was then advanced through the sacral hiatus under fluoroscopic image guidance, and the epidural space was identified by injecting diluted contrast medium. According to the symptom-

atology and MRI results, an epidural inflatable balloon catheter (ZiNeu®, JUVENUI) was inserted through the guide needle and positioned at the location of the filling defect or the pathological site after an epidurogram was performed to identify target areas. Percutaneous epidural neuroplasty using a balloon catheter was performed to target sites such as the central canal, lateral recess, and intervertebral foramen. With each ballooning procedure lasting no more than 5 seconds, the balloon was softly inflated with 0.13 mL of contrast media using a 1-mL Luer-Lock syringe. The balloon catheter was only transferred in the deflated state to prevent severe pain or injury if the patient reported moderate to severe pain while the balloon was being inflated, and no additional decompression (ballooning) attempts were made. After adhesiolysis and decompression, a total of 10 mL of 1% lidocaine mixed with 1,500 IU hyaluronidase and 5 mg dexamethasone was administered at each target site after excluding subarachnoid or intravascular filling with contrast agents. At the end of the procedure, an additional epidural catheter was inserted at the main target site through the ZiNeu catheter, and 4 mL of 10% hypertonic saline was injected *via* the epidural catheter in the recovery room. The catheter was kept in place for a 2-day drug injection regimen. The catheter was then removed on the next day of the procedure after the same drugs (after a test injection of 2 mL of 1% lidocaine, 4 mL of 10% hypertonic saline with 5 mg dexamethasone) were injected again.

After performing percutaneous epidural neuroplasty using a balloon catheter, periodic follow-ups were performed. During follow-ups, additional interventional treatment was planned in the following cases: (1) the patient's symptoms did not improve or become more severe, (2) additional drug prescriptions were not effective, or (3) patients who had improved symptoms but were not satisfied.

3. Demographic data and outcome assessments

Prior to the procedure, all patients learned how to evaluate the severity of their leg or lower back pain using an 11-point NRS. Baseline characteristics, which included age, sex, body mass index (BMI), hypertension, diabetes, pain duration, location, intensity, and medications, were retrieved from electronic medical records. The location, grade, and total number of LSS (central and foraminal) and spondylolisthesis were recorded from MRI images using a photo archiving and communication system (PetaVision, Version 2.1, Seoul, Korea) [18–21]. The presence of spondylolisthesis was measured on mid-sagittal images of the lumbar column and analyzed by a consensus among the three investigators (two pain physicians and one radiologist with more than 10 years of experience in the clinical field). Intervention characteristics, including target level and complications, were also recorded. The medication quantification scale III (MQS) was used to quantify changes in analgesics, and opioid use was also examined [22]. At baseline and at 1, 3, and 6 months following the procedure, all altered data (improvement in NRS score, change in MQS for pain control and symptom management, and improved physical functional status) were gathered. Improvement in physical functional status was defined as an amelioration of the activities of daily living and an increase in walking distance [17]. Adverse events and follow-up data during the treatment were individually recorded. Chronic LSS patients were divided with accompanying DLS (the spondylolisthesis group) and those without DLS (the no spondylolisthesis group) to evaluate whether the effects of percutaneous epidural neuroplasty using a balloon catheter were different.

4. Statistical analysis

If a continuous variable is skewed, the median and interquartile range are shown, otherwise the mean and standard deviation. Frequencies and percentages are used to present categorical variables. Continuous variables were compared between the two groups' baselines using the Student's *t*-test or Mann–Whitney *U*-test, as appropriate. To properly analyze the between-group differences, categorical variables were compared with Fisher's exact tests or Pearson's chi-square tests.

To replace missing data at the six-month follow-up, a generalized estimating equations (GEE) model was used. Stata version 13.1 (StataCorp LP, College Station, TX) and IBM SPSS Statistics for Windows, version 22.0 (IBM Corp., Armonk, NY), were used for data manipulation and statistical analysis. The threshold for statistical significance was established at $P = 0.05$, and all reported P values were two-sided.

RESULTS

During the study period, 1,218 patients who had undergone percutaneous epidural neuroplasty using a balloon catheter were collected in the entire cohort, of whom 392 were excluded based on the exclusion criteria. Among these 392 excluded patients, 143 had undergone lumbar spine surgery before or after percutaneous epidural

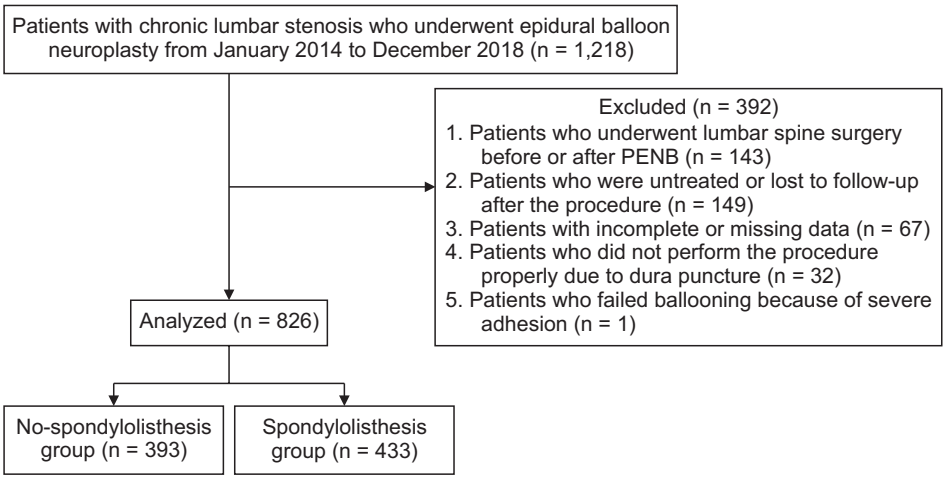

Fig. 1. A flow diagram of the study population. PENB: percutaneous epidural neuroplasty using a balloon catheter.

neuroplasty using a balloon catheter, 149 were lost to follow-up, 67 had missing baseline data, 32 had dura puncture during percutaneous epidural neuroplasty using a balloon catheter, and one had failed ballooning due to severe adhesion. Finally, this study included a total of 826 patients who were divided into spondylolisthesis (433 patients, 52.4%) and no spondylolisthesis (393 patients, 47.6%) groups (**Fig. 1**). **Table 1** shows the baseline and intervention characteristics of the study population. The median NRS score of pain intensity was 7.0 (6.0–8.0) for both back and leg pain. The median values of MQS and pain duration of the total study population were 8.3 and 24 months, respectively. Age, BMI, hypertension, and location of pain had statistically considerable differences between the two groups. In stenosis grading, both severe central and foraminal stenosis were significantly higher in the spondylolisthesis group. In the spondylolisthesis group, 236 patients (54.5%) had anterolisthesis, 167 patients (38.6%) had retrolisthesis, and 30 patients (6.9%) had both. A total of 307 (70.9%) patients had one level of spondylolisthesis, 91 patients (21.0%) had two levels of spondylolisthesis, and 35 patients (8.1%) had three or more levels of spondylolisthesis. The level of spondylolisthesis was L1-2 in eight patients (1.3%), L2-3 in 69 patients (11.5%), L3-4 in 134 patients (22.3%), L4-5 in 256 patients (42.6%), and L5-S1 in 134 patients (22.3%). Grade 1 and 2 spondylolisthesis was observed in 423 patients (97.7%) and 10 (2.3%), respectively. **Table 2** shows the target site, target level, and their number. There was no statistically significant difference in the target site, target level, and their number between the two groups.

The unadjusted estimation of values and differences between the no spondylolisthesis and spondylolisthesis groups from baseline for the NRS scores of leg and back pain and MQS over the six months follow-up period are shown in **Table 3**. GEE analysis revealed a considerable improvement in the estimated mean NRS score of pain intensities compared to that at baseline throughout the study period in both groups ($P < 0.001$). When comparing the two groups using a GEE model, there were no significant differences in the NRS scores for leg and back pain. No significant differences were found between the groups regarding an improvement in mean MQS compared to that at baseline. The *P* values of the interactions between the groups and times for back pain, leg pain, and MQS were 0.214, 0.081, and 0.616, respectively (**Table 3**).

For the NRS scores for pain and MQS over the six-month follow-up period, the adjusted estimation of values and differences between the two groups from baseline are displayed in **Table 4**. Age, sex, BMI, diabetes, hypertension, central stenosis grading, and foraminal stenosis grading were included to adjust for demographic differences. In both groups, GEE analyses also revealed a significant improvement in the adjusted estimation of mean NRS score compared to that at baseline ($P < 0.001$). There were no significant between-group differences in leg and back pain NRS scores or mean MQS compared to those at baseline. The *P* values of the interactions between the groups and times for back pain, leg pain, and MQS were 0.456, 0.152, and 0.975, respectively (**Table 4**).

The estimated proportions of improved physical function over the six-month period after percutaneous epidural neuroplasty using a balloon catheter in both groups are shown in **Table 5**. There was no statistically considerable difference in physical functional status between the two groups. The adjusted *P* value of the interaction between the groups and time for physical functional status was 0.831 (**Table 5**).

Table 1. Baseline characteristics of the study population

Variables	Total (n = 826)	Spondylolisthesis		*P* value
		No (n = 393)	Yes (n = 433)	
Age (yr)	67.5 (61.0–74.0)	66.0 (59.0–73.0)	68.0 (62.0–75.0)	0.002
Sex, male	400 (48.4)	201 (51.1)	199 (46.0)	0.136
BMI (kg/m^2)	24.52 (22.70–26.53)	24.42 (22.53–26.33)	24.76 (22.89–26.63)	0.045
Diabetes	160 (19.4)	85 (21.6)	74 (17.1)	0.134
Hypertension	358 (43.3)	155 (39.4)	203 (46.9)	0.035
Pain duration (mo)	24.00 (12.00–48.00)	22.00 (10.00–50.00)	24.00 (12.00–48.00)	0.294
Pain location				0.025
Back	63 (7.6)	20 (5.1)	43 (9.9)	
Leg	242 (29.3)	123 (31.3)	119 (27.5)	
Both	521 (63.1)	250 (63.6)	271 (62.6)	
Pain intensity (NRS)				
Back pain	7.00 (6.00–8.00)	7.00 (6.00–8.00)	7.00 (6.00–8.00)	0.790
Leg pain	7.00 (6.00–8.00)	7.00 (6.00–8.00)	7.00 (6.00–8.00)	0.096
MQS	8.30 (4.20–12.40)	8.30 (4.20–12.80)	8.40 (4.20–12.25)	0.574
Central stenosis grading				< 0.001
Mild	238 (28.8)	141 (35.9)	97 (22.4)	
Moderate	160 (19.4)	75 (19.1)	85 (19.6)	
Severe	381 (46.1)	156 (39.7)	225 (52.0)	
Foraminal stenosis grading				0.001
Mild	254 (30.8)	139 (35.4)	115 (26.6)	
Moderate	207 (25.1)	110 (28.0)	97 (22.4)	
Severe	215 (26.0)	84 (21.4)	131 (30.3)	

Values are expressed as medians (interquartile ranges) or numbers (%).
BMI: body mass index, NRS: numerical rating scale, MQS: medication quantification scale.

Although some patients had complications, such as vascular injection, decreased blood pressure, and transient motor weakness, there were no severe adverse effects reported. All adverse events that happened during the study period were temporary and minor. Thirty-two patients with dura mater puncture were excluded from the analysis. None of the 32 patients who had dura puncture during the procedure complained of post-dural puncture headache or subdural hematoma. Among the 826 participants, a total of 15 (1.9%) complications occurred. In the spondylolisthesis group, three patients had vascular injections, two patients had transient motor weakness, and five patients had hypotension. In the no spondylolisthesis group, one patient had transient motor weakness, and four patients had transient hypotension. Between the two groups, there were no considerable differences in adverse events. There were no additional adverse events such as prolonged sensory or motor impairments or infection. During the follow-up period of six months after the percutaneous epidural neuroplasty using a balloon catheter, a total of 234 (28.3%) patients underwent additional interventional procedures. However, there was no significant difference between the two groups (**Table 6**). In addition, among the patients who received additional treatment, 27 (6.9%) patients in the no spondylolisthesis group and 31 (7.2%) patients in the spondylolisthesis group underwent 2 or more additional procedures during follow-up period ($P = 0.979$).

DISCUSSION

The results of this study demonstrated that percutaneous epidural neuroplasty using a balloon catheter reduced pain severity and improved physical functional status for at least six months in patients with chronic LSS regardless of DLS. There was no statistically considerable difference in clinical outcomes between the two groups.

DLS is a common cause of low back pain, particularly in the elderly, and affects about 11.5% of people in the

Table 2. Intervention characteristics of the study population

Variables	Total (n = 826)	Spondylolisthesis		*P* value
		No (n = 393)	Yes (n = 433)	
Target site				0.144
Foraminal (Lt/Rt/both)	152/149/89 (18.4/18.0/10.8)	77/76/36 (19.6/19.3/9.2)	75/73/53 (17.3/16.9/12.2)	
Central	167 (20.2)	69 (17.6)	98 (22.6)	
Foraminal (Lt/Rt/both) with central	81/59/129 (9.8/7.1/15.6)	45/24/66 (11.5/6.1/16.8)	36/35/63 (8.3/8.1/14.5)	
Number of target level				0.055
1 level	398 (48.2)	174 (44.3)	224 (51.7)	
2 levels	344 (41.6)	170 (43.3)	174 (40.2)	
3 levels	76 (9.2)	44 (11.2)	32 (7.4)	
4 levels or more	8 (1.0)	5 (1.3)	3 (0.7)	
Target level[a]				
L3	10	4	6	0.629
L4	119	62	57	0.286
L5	611	302	309	0.073
S1	32	20	12	0.085
L2-3	1	0	1	0.340
L3-4	7	2	5	0.312
L4-5	267	116	151	0.100
L5-S1	35	20	15	0.247
L2-3-4	2	1	1	0.945
L3-4-5	45	24	21	0.427
L4-5-S1	68	31	37	0.732
L2-3-4-5	2	1	1	0.945
L3-4-5-S1	12	9	3	0.055

Values are expressed as numbers (%) or number only.

[a]When multiple sites were targeted on one patient, it was counted as duplicates.

United States [23]. Several studies have recommended that patients with low-grade DLS who have radiculopathy and/or pseudoclaudication may be considered for 3–6 months of conservative therapy, such as exercise, physical therapy, medications, and ESI [24]. When conservative therapy has failed, surgical intervention may be considered [25–28]. Evidence shows superior results for patients with DLS who undergo surgical treatment compared to those who receive nonsurgical treatment [5]. Even if surgical treatment is effective, due to their limited physical status, older patients with a variety of comorbidities may not always be surgical candidates, and spine degeneration may still progress even after surgery. Surgical intervention is not the answer in all patients who have failed to improve with conservative therapies. In fact, patients < 65 years of age were found to have a higher treatment benefit with surgery compared to that in those ≥ 65 years [24]. The mean age of the patients analyzed was 67.5 years, and patients with DLS were significantly older than patients without DLS (P = 0.002). The median age in the no spondylolisthesis group was 66 years. It is worthy of consideration that non-surgical treatment may be more appropriate for the patients in this study's cohort.

Regarding demographic data (**Table 1**), BMI, hypertension, pain location, LSS grade, and age were statistically different between the two groups. DLS is a degenerative disease similar to LSS, and its prevalence is higher in the elderly [24]. The grade of stenosis was increased in the spondylolisthesis group, which included the elderly. Since the proportion of severe central stenosis in the spondylolisthesis group was relatively high, it was considered that the proportion of back pain was higher among those with spondylolisthesis than among those without it. Because the prevalence of hypertension also increases

Table 3. Changes in the estimated pain scores and medication quantification scores after percutaneous epidural neuroplasty using a balloon catheter in patients with chronic spinal stenosis with and without spondylolisthesis

Variables	Time	Estimated means (95% CI)		Estimated difference (95% CI)[a]	*P* value
		No-spondylolisthesis (n = 393)	Spondylolisthesis (n = 433)		
Back pain (NRS)	Baseline	6.8 (6.5–7.0)	6.6 (6.4–6.8)	–0.2 (–0.5–0.2)	0.355
	1 month	4.8 (4.5–5.0)[b]	4.7 (4.5–4.9)[b]	–0.1 (–0.4–0.3)	0.761
	3 months	4.8 (4.4–2.1)[b]	4.4 (4.1–4.8)[b]	–0.3 (–0.8–0.1)	0.152
	6 months	4.2 (3.7–4.6)[b]	4.6 (4.1–5.0)[b]	0.4 (–0.2–1.0)	0.228
Leg pain (NRS)	Baseline	7.0 (6.8–7.2)	7.2 (7.0–7.4)	0.2 (–0.1–0.5)	0.206
	1 month	4.8 (4.6–5.1)[b]	4.9 (4.6–5.1)[b]	0.0 (–0.3–0.3)	0.904
	3 months	4.8 (4.5–5.1)[b]	4.4 (4.1–4.7)[b]	–0.3 (–0.8–0.1)	0.100
	6 months	4.4 (4.0–4.8)[b]	4.6 (4.2–5.0)[b]	0.2 (–0.3–0.7)	0.507
MQS	Baseline	8.6 (7.9–9.3)	8.1 (7.5–8.8)	–0.5 (–1.4–0.5)	0.316
	1 month	8.9 (8.2–9.6)	8.7 (8.0–9.3)	–0.2 (–1.1–0.7)	0.631
	3 months	9.2 (8.5–10.0)	8.4 (7.7–9.1)	–0.8 (–1.8–0.2)	0.111
	6 months	8.2 (7.3–9.0)	7.9 (7.2–8.7)	–0.2 (–1.3–0.9)	0.675

A NRS was used to assess the intensity of both lower back and leg pain. A generalized estimating equations model was used in the statistical analysis. Data are presented as the estimated mean with 95% CI. The *P* values of the interactions between the groups and times were 0.214, 0.081, and 0.616 for back pain, leg pain, and MQS, respectively.

CI: confidence interval, NRS: numerical rating scale, MQS: medication quantification scale.

[a]Estimated difference in values between groups.

[b]$P < 0.001$ compared to baseline in each group.

Table 4. Adjusted changes in the estimated pain scores and medication quantification scores after percutaneous epidural neuroplasty using a balloon catheter in patients with chronic spinal stenosis with and without spondylolisthesis

Variables	Time	Estimated means (95% CI)		Estimated difference (95% CI)[a]	*P* value
		No-spondylolisthesis (n = 393)	Spondylolisthesis (n = 433)		
Back pain (NRS)	Baseline	6.9 (6.6–7.2)	7.0 (6.7–7.3)	0.1 (–0.3–0.5)	0.617
	1 month	4.8 (4.5–5.1)[b]	4.9 (4.6–5.1)[b]	0.1 (–0.4–0.5)	0.812
	3 months	5.0 (4.6–5.4)[b]	4.7 (4.4–5.1)[b]	–0.2 (–0.8–0.3)	0.378
	6 months	4.6 (4.1–5.1)[b]	4.9 (4.5–5.4)[b]	0.3 (–0.4–1.0)	0.348
Leg pain (NRS)	Baseline	7.0 (6.7–7.3)	7.3 (7.0–7.5)	0.3 (–0.1–0.7)	0.164
	1 month	4.8 (4.6–5.1)[b]	4.9 (4.6–5.2)[b]	0.0 (–0.3–0.4)	0.849
	3 months	4.8 (4.5–5.2)[b]	4.5 (4.2–4.9)[b]	–0.3 (–0.8–0.2)	0.252
	6 months	4.6 (4.2–5.0)[b]	4.8 (4.4–5.2)[b]	0.2 (–0.4–0.8)	0.484
MQS	Baseline	9.6 (8.8–10.5)	9.0 (8.1–9.8)	–0.6 (–1.8–0.5)	0.290
	1 month	9.5 (8.7–10.4)	9.1 (8.3–9.9)	–0.4 (–1.6–0.8)	0.497
	3 months	9.6 (8.7–10.5)	9.2 (8.3–10.1)	–0.4 (–1.7–0.9)	0.549
	6 months	9.1 (8.0–10.1)	8.6 (7.7–9.6)	–0.4 (–1.9–1.0)	0.544

A NRS was used to assess the intensity of both lower back and leg pain. A generalized estimating equations model was used in the statistical analysis. Age, sex, body mass index, hypertension, location of pain, central stenosis grading, and foraminal stenosis grading were included to adjust for demographic differences. Data are presented as estimated mean with 95% CI. The *P* values of the interactions between the groups and times were 0.456, 0.152, and 0.975 for back pain, leg pain, and MQS, respectively.

CI: confidence interval, NRS: numerical rating scale, MQS: medication quantification scale.

[a]Estimated difference in values between groups.

[b]$P < 0.001$ compared to baseline in each group.

Table 5. Estimated proportion of improved function after percutaneous epidural neuroplasty using a balloon catheter in patients with chronic spinal stenosis with and without spondylolisthesis

Variables	Time	Estimated proportion (95% CI)		Estimated difference (95% CI)[a]	*P* value	Adjusted *P* value[b]
		No-spondylolisthesis (n = 393)	Spondylolisthesis (n = 433)			
Function	1 month	0.6 (0.6–0.7)	0.7 (0.6–0.7)	0.2 (–0.2–0.5)	0.315	0.904
	3 months	0.6 (0.6–0.7)	0.7 (0.6–0.7)	0.2 (–0.2–0.5)	0.406	0.534
	6 months	0.6 (0.5–0.7)	0.6 (0.6–0.7)	0.1 (–0.3–0.5)	0.649	0.515

Data are presented as the estimated proportions with 95% CIs. A generalized estimating equations model was used in the statistical analysis.
CI: confidence interval.
[a]Estimated difference in values between groups.
[b]Adjusted *P* values considering age, sex, body mass index, hypertension, location of pain, central stenosis grading, and foraminal stenosis grading as covariates. The adjusted *P* value of the interaction between the group and time was 0.831.

Table 6. Additional interventional procedures in the 6-month follow-up period for the study population

Additional procedures	No-spondylolisthesis (n = 393)	Spondylolisthesis (n = 433)	*P* value
Interlaminar epidural block	91 (23.2)	94 (21.7)	0.679
Transforaminal epidural block	34 (8.7)	27 (6.2)	0.233
Caudal epidural block	9 (2.3)	9 (2.1)	> 0.999
Epidural balloon neuroplasty	31 (7.9)	22 (5.1)	0.133
Neuroplasty without balloon	5 (1.3)	5 (1.2)	> 0.999
Pulsed radiofrequency	8 (2.0)	15 (3.5)	0.301
Others[a]	16 (4.1)	25 (5.8)	0.335

Data are expressed as number (%). During the 6 months follow-up period after the percutaneous epidural neuroplasty using a balloon catheter, 234 (28.3%) patients underwent additional interventional procedures. Among the patients who received additional treatment, 27 (6.9%) patients in the no-spondylolisthesis group and 31 (7.2%) patients in the spondylolisthesis group underwent 2 or more procedures (*P* = 0.979).
[a]Others included ketamine infusion therapy, lumbar sympathetic block, medial branch block, nucleoplasty, percutaneous endoscopic lumbar decompression, piriformis injection, prolotherapy, and trigger point injection.

in the elderly [29], it was thought that the spondylolisthesis group had a higher prevalence of hypertension than the no spondylolisthesis group. Although there was no difference in the prevalence of diabetes between the two groups, previous studies have concluded that spine patients with diabetes, including those with DLS, were significantly older and had a higher BMI and an increased prevalence of hypertension, cardiovascular disease, stroke, and joint disease compared to patients without diabetes [30]. In addition, diabetes may be a poor prognostic factor for percutaneous epidural neuroplasty using a balloon catheter [13].

To the authors' knowledge, no research has reported the effectiveness of percutaneous epidural neuroplasty using a balloon catheter in patients with LSS accompanying DLS. One study found that DLS may be associated with unsuccessful outcomes of percutaneous epidural neuroplasty with a balloonless catheter [16]. Interestingly, the results of this study demonstrated an improvement in pain and physical functional status at 1-, 3-, and 6-months of follow-ups in patients with chronic LSS regardless of DLS. Percutaneous epidural neuroplasty using a balloon catheter was recently developed for safe and successful epidural decompression and adhesiolysis [12,13,31], and shows an excellent therapeutic effect in patients with intractable low back and radicular pain [11,14,15]. Percutaneous epidural neuroplasty using a balloon catheter provides significant pain reduction and functional improvement compared to conventional neuroplasty with balloonless catheters in patients with chronic LSS [11,14]. Although not fully understood, the following mechanisms may provide evidence for the effectiveness of percutaneous epidural neuroplasty using a balloon catheter. First, it may decrease the pain intensity of patients with LSS due to the advantages of balloon inflation/deflation, which offers a combination of mechanical effects, such as adhesion, removal and decompression. Second, chemical effects of using the

medications, such as local anesthetics, steroids, and hypertonic saline, may also contribute to an effect. Third, because of its maneuverability and ballooning, percutaneous epidural neuroplasty using a balloon catheter may more effectively deliver drugs to the target lesion site. In patients with chronic LSS accompanied by DLS, accurate drug injection may be difficult due to severe adhesions and anatomical displacement to the target lesion site. Because the balloon catheter may be moved both vertically and horizontally, physicians can more easily place the catheter at the sites of target lesions. Additionally, the thin epidural catheter can be left in place at the site of the target lesion for a number of days, allowing for epidural medication injections [11,14,15]. Fourthly, local anesthetics stabilize the sensitized nerves and decrease the excitability of sympathetic nerve fibers [32], while steroids have anti-inflammatory actions [33]. Finally, hypertonic saline reduces neural activity and cell edema, and has an analgesic effect by expressing a hyperosmolar effect through the semipermeable membrane of the nerve root [34].

This study had several limitations. First, chronic pain assessment requires considering multidimensional qualitative factors, such as pain intensity, physical function, emotional function, and analgesic effect [35]. However, the pain assessment in this study included only pain intensity, physical function, and analgesic effect (*i.e.*, it did not include emotional function). Second, an improvement in physical function was considered an amelioration of the activities of daily living and walking distance in this study. It would have been more appropriate to use a tool like the Oswestry Disability Index [36], but this was not possible due to the retrospective nature of the study. However, the definition of an improvement in physical functional status was established based on a previous study [15,17] and the response criteria was carefully designated to reflect the clinically meaningful functional status of patients. Third, information on adjuvant nonpharmacologic therapies, such as exercise therapy and physical therapy, were lacking in individual patients. Finally, the retrospective design might have led to the reporting of undocumented factors or biases. However, the authors tried to minimize the impact of confounding factors by using GEE to adjust for variables that might have affected the outcome. It is necessary to conduct randomized controlled trials using appropriate selection criteria to evaluate the outcomes of this therapeutic approach.

In conclusion, percutaneous epidural neuroplasty using a balloon catheter may lead to considerable pain reduction and functional improvement for at least six months in patients with chronic LSS including those with accompanying DLS. Percutaneous epidural neuroplasty using a balloon catheter may be an alternative method of treatment for patients with chronic LSS with DLS for whom conservative management has failed.

DATA AVAILABILITY

The corresponding author can provide the datasets that support the study's findings upon reasonable request.

ACKNOWLEDGMENTS

The authors appreciate Dr. Seong-Sik Cho, MD, MPH, PhD (the Department of Occupational and Environmental Medicine, College of Medicine, Dong-A University, Busan, Korea) for the statistical support. The authors would like to thank residents in the Department of Anesthesiology and Pain Medicine, the Asan Medical Center for assistance of data collection in this study. The authors would like to thank Dental Research Institute of Seoul National University for the English language review.

CONFLICT OF INTEREST

One of the authors created the ZiNeu® catheter and gave the patent to JUVENUI Co., Ltd. before planning this study. There are no disclosed conflicts of interest for the other authors.

FUNDING

No funding to declare.

AUTHOR CONTRIBUTIONS

Myong-Hwan Karm: Writing/manuscript preparation; Chan-Sik Kim: Writing/manuscript preparation; Doo-Hwan Kim: Investigation; Dongreul Lee: Investigation; Youngmu Kim: Investigation; Jin-Woo Shin: Study conception; Seong-Soo Choi: Study conception.

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