Randomized Trial

Percutaneous Epidural Adhesiolysis Using Inflatable Balloon Catheter and Balloon-less Catheter in Central Lumbar Spinal Stenosis with Neurogenic Claudication: A Randomized Controlled Trial

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Background: When conventional interventional procedures fail, percutaneous epidural adhesiolysis (PEA), which has moderate evidence for successful treatment of lumbar spinal stenosis (LSS), has been recommended over surgical treatments. In a previous study, we demonstrated the efficacy of a newly developed inflatable balloon catheter for overcoming the access limitations of pre-existing catheters for patients with severe stenosis or adhesions.

Objectives: This study compared the treatment response of combined PEA with balloon decompression and PEA only in patients with central LSS over 6 months of follow-up.

Study Design: This study used a randomized, single-blinded, active-controlled trial design.

Setting: This study took place in a single-center, academic, outpatient interventional pain management clinic.

Methods: This randomized controlled study included 60 patients with refractory central LSS who suffered from chronic lower back pain and/or lumbar radicular pain. Patients failed to maintain improvement for > 1 month with epidural steroid injection or PEA using a balloon-less catheter. Patients were randomly assigned to one of 2 interventions: balloon-less (n = 30) and inflatable balloon catheter (n = 30). The Numeric Rating Scale (NRS-11), Oswestry Disability Index (ODI), Global Perceived Effect of Satisfaction (GPES), and Medication Quantification Scale III were each measured at 1, 3, and 6 months after PEA.

Results: There was a significant difference between groups in NRS-11 reduction ≥ 50% (or 4 points), ODI reduction ≥ 30% (or 10 points), GPES ≥ 6 and ≥ 4 points at 6 months, and NRS-11 reduction ≥ 50% (or 4 points) at 3 months after PEA ($P < .03$). The proportion of successful responders was higher in the balloon group than in the balloon-less group throughout the total follow-up period. Furthermore, there was a statistically significant difference between groups at 6 months after PEA ($P = .035$).

Limitations: The results may vary according to the definition of successful response. Follow-up loss in the present study seemed to be high.

Conclusion: PEA using the inflatable balloon catheter leads to significant pain reduction and functional improvement compared to PEA using the balloon-less catheter in patients with central LSS.

The study protocol was approved by our institutional review board (2012-0235), and written informed consent was obtained from all patients. The trial was registered with the Clinical Research Information Service (KCT 0002093).

Key words: Balloon decompression, central, chronic pain, epidural adhesiolysis, lumbar, percutaneous, radiculopathy, spinal stenosis

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Spinal stenosis was first defined by Verbiest as a narrowing of the spinal canal producing radiculopathy or claudication, which are common findings in the degenerative spine (1). Lumbar spinal stenosis (LSS) is one of the most common causes of chronic lower back pain and leg pain in individuals of advanced age (2). LSS is important because it is socially disabling and economically expensive (3). Nonsurgical treatments (such as exercise, medical treatment, physical therapy, and conventional interventional procedures) for initial management of LSS have been recommended (4,5). However, these treatments have limitations, and even conventional interventional procedures, such as epidural steroid injection (ESI), are occasionally ineffective for pain and functional disability in patients with LSS (6,7). Because individuals of advanced age with various comorbidities are not always surgical candidates due to their limited physical status, surgery is not the solution in all patients nonresponsive to nonsurgical treatments. Therefore, when conventional interventional procedures fail, percutaneous epidural adhesiolysis (PEA), which has moderate evidence for successful treatment of LSS, has been recommended over surgical treatments (8-12).

Generally, PEA is performed with a Racz catheter or a more steerable navigation catheter (NaviCath) (4,13-15). In a previous study, we demonstrated the efficacy of a newly developed inflatable balloon catheter (ZiNeu®, JUVENUI, Seoul, Korea) for overcoming the access limitations of pre-existing catheters for patients with severe stenosis or adhesions (16,17). It has been suggested that the ZiNeu catheter could be an alternative to other PEA catheters in patients with failure to sufficiently relieve stenosis or remove adhesions. However, there is no randomized, single-blinded, active-controlled study of Racz and ZiNeu catheter efficacy for PEA treatment in patients with LSS.

We hypothesized that the use of the ZiNeu catheter for PEA would increase the treatment response compared to the Racz catheter in patients with central LSS. In the present randomized controlled study, we evaluated the effects of 6 months of combined PEA with balloon decompression (ZiNeu catheter) compared to PEA only (Racz catheter) for patients presenting chronic lower back pain and/or leg pain caused by degenerative central LSS.

Methods

Study Design and Participants

This randomized, single-blinded, active-controlled study was conducted at the pain management clinic of our center. Permission to conduct this study was granted by our Institutional Review Board (approval number: 2012-0235), and written informed consent was obtained from each patient who participated in this study. All aspects of patient privacy and confidentiality were preserved. This study was registered with the Clinical Research Information Service (cris.nih.go.kr/KCT0002093) and conducted in accordance with the Declaration of Helsinki (18). We followed the CONSORT guidelines to report this study.

Chronic LSS patients who visited the pain management clinic in our center between January 2014 and June 2016 were examined to ascertain their eligibility. Inclusion criteria were as follows: (1) chronic LSS patients aged ≥ 40 years; (2) lower back pain and/or lumbar radicular pain intensity ≥ 6 (out of 10) on the Numerical Rating Scale (NRS-11), and neurogenic intermittent claudication; (3) confirmed diagnosis of moderate or severe central, but not foraminal or lateral recess, LSS by magnetic resonance imaging (MRI) (19); and (4) previous failure of conservative management, such as exercise therapy, physical therapy, or analgesic medication. ESI or PEA using a balloon-less catheter ≥ 12 weeks before recruitment was permitted because most of the patients visiting our clinic had a history of epidural injections. All eligible patients received a conventional diagnostic/therapeutic fluoroscopy-guided transforaminal, interlaminar, caudal epidural injection with local anesthetic and steroid administration before enrollment. Patients who showed no or minimal pain reduction response (< 50%) for < 1 month {AU: checking – should this be > 1 month?} following ESI or PEA using a balloon-less catheter (Racz or NaviCath) were enrolled.

Exclusion criteria were as follows: (1) age < 40 years, (2) acute pain for < 3 months, (3) unbearable pain of 10 points on the NRS-11, (4) axial pain associated with facet joint or somatic origin, (5) cannot exclude a confounding diagnosis of vascular disease or disease of other origins, (6) signs of progressive neurological deficits or motor weakness, including muscle atrophy and abnormal tendon reflexes, (7) allergies to steroids or contrast dyes, (8) coagulopathy, (9) uncontrollable or unstable opioid use, (10) pregnancy or lactation, (11) malignancy, (12) systemic or injection site infection, (13) a history of prior lumbar spine surgery, (14) central LSS at ≥ 4 levels, and (15) unstable medical or psychiatric condition.

Randomization and Blinding

Patients were randomly assigned to one of two

groups: the Racz (balloon-less) group (n = 30) or the ZiNeu (inflatable balloon) group (n = 30). An independent data manager assigned the patients to groups based on a computer-generated randomization program. The study patients and the outcome assessor, who was an independent physician from the outpatient pain management clinic, were blinded to each patient's randomization number.

Intervention: Percutaneous Epidural Decompression and Adhesiolysis Using an Inflatable Balloon Catheter (ZiNeu)

All procedures in this study were performed by 2 pain specialists with > 5 years of experience on an outpatient basis, and no premedication or sedatives were used. Before the procedure, intravenous access was achieved, antibiotics were administered, and fluoroscopic guidance was implemented in all cases. A single fluoroscopy C-arm system (OEC 9800, General Electric Healthcare, Little Chalfont, United Kingdom) was used. Each patient was placed in the prone position with a pillow under the abdomen to minimize lumbar lordosis, and vital parameters were monitored (blood pressure, electrocardiogram, and pulse oximeter) during the procedure. After sterile preparation for the procedure, both the skin and soft tissues were infiltrated with 1% lidocaine. A 10-guage guide needle, which was custom designed to prevent cutting or skiving of the catheter, was inserted into the epidural space through the sacral hiatus under intermittent fluoroscopy. The epidural space was identified on the basis of the injection of approximately 8 mL of diluted contrast medium (Omnipaque, Nycomed Imaging AS, Oslo, Norway) under fluoroscopy. The diluted contrast mixture was composed of approximately 4 mL of pure contrast medium, 4 mL of 1% lidocaine, and 1500 IU of hyaluronidase. Filling defects were identified by examining the contrast flow. If intravascular or subarachnoid placement of the needle or contrast occurred, the needle was removed and repositioned.

After appropriate determination of the epidurogram and target areas, a ZiNeu catheter was advanced through the guide needle to the area of the filling defect or to the site of pathology, as determined by MRI or symptomatology. Gentle mechanical adhesiolysis and epidural decompression were performed with the ZiNeu catheter at the appropriate target sites (the central ventral and/or dorsal epidural spaces). Epidural decompression and adhesiolysis were performed using gentle side-to-side movement of the catheter with intermittent ballooning. The balloon was then filled with 0.13 mL of contrast agent using a 1-mL Luer–Lock syringe (BD Medical, Franklin Lakes, NJ), and each ballooning process was limited to 5 seconds. The extent of balloon inflation was adjusted according to the degree of pain; if moderate to severe pain was noted during balloon inflation, no further attempt was made because of safety concerns. The catheter was only moved in the deflated state. After adhesiolysis and decompression, 1 mL of pure contrast was injected to identify subarachnoid or intravascular filling as well as to ensure satisfactory filling of the previous defects (Fig. 1). Then, a total of 5 mg of dexamethasone in 1% lidocaine was injected at each target site with a volume of 2 mL each. At the end of the procedure, a Perifix epidural catheter (B. Braun Melsungen AG, Melsungen, Germany) was retained at the main target site through the ZiNeu catheter lumen. After confirming the position of the Perifix catheter tip, the ZiNeu catheter was removed. The catheter was fixed with bio-occlusive dressing. In the recovery room, a test injection of 2 mL of 1% lidocaine was administered through the Perifix catheter. After 10–15 minutes of monitoring, another 4 mL of 10% hypertonic saline was injected through the Perifix catheter. The Perifix catheter was left in place for a 2-day drug-injection regimen. The catheter was removed on the second day after the procedure after the same drugs (2 mL of 1% lidocaine, a total of 5 mg dexamethasone, and 4 mL of 10% hypertonic saline) were injected. The administration of the drug on the second day was performed on an outpatient basis and the patient was discharged after confirming that there was no complication.

Intervention: PEA Using a Balloon-less Catheter (Racz)

Similar to the ZiNeu procedure, after preparation for the procedure a 15-gauge RK needle (Epimed International, Inc., Gloversville, NY) was inserted into the epidural space through the sacral hiatus under intermittent fluoroscopy, and a 19-gauge Racz catheter was advanced through the needle up to the third sacral vertebra. An epidurogram was then obtained by injecting 5 mL of contrast medium; filling defects were identified by examining the contrast flow. If intravascular or subarachnoid placement of the needle or contrast occurred, the needle was removed and repositioned.

After appropriate determination of the epidurogram and target areas, a Racz catheter was advanced through the guide needle to the area of the filling de-

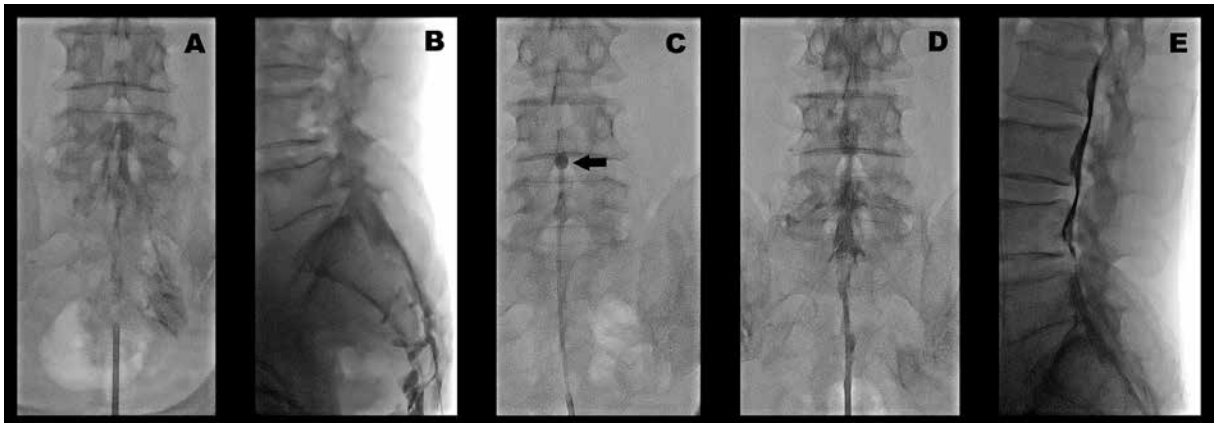

Fig. 1. *A serial fluoroscopic image of lumbar spine during percutaneous epidural adhesiolysis (PEA) using an inflatable balloon catheter (ZiNeu). (A, B) Anteroposterior and lateral views verified before the procedure showing filling defects of contrast medium at the epidural space at L4-5 intervertebral disc level. (C) Fluoroscopic view showing the inflatable balloon neuroplasty catheter placed at L4-5 intervertebral disc level and the balloon filled with contrast medium (arrow). (D, E) After balloon decompression and PEA along the pass from the L5 to the L4 vertebra level, the contrast agent spread well to L2 vertebra level.*

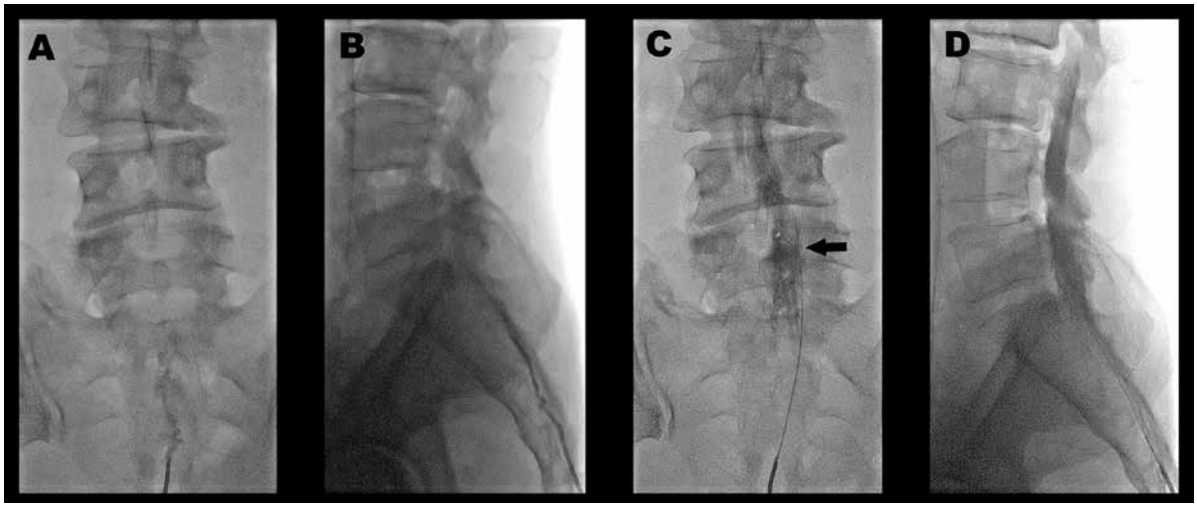

Fig. 2. *A serial fluoroscopic image of lumbar spine during percutaneous epidural adhesiolysis (PEA) using a balloon-less catheter (Racz). (A, B) Anteroposterior and lateral views verified before the procedure showing filling defects of contrast medium at the epidural space at L5-S1 intervertebral disc level. (C, D) Fluoroscopic view showing the Racz catheter passed through L5-S1 intervertebral disc level and placed at L4-5 intervertebral disc level (arrow). After the procedure, the contrast agent spread well to L3 vertebra level.*

fect or to the site of pathology, as determined by MRI or symptomatology. Gentle adhesiolysis was performed at the appropriate target sites (the central ventral and/or dorsal epidural spaces). After adhesiolysis, 1 mL of pure contrast was injected to detect subarachnoid or intravascular filling as well as to ensure satisfactory filling of the previous defects (Fig. 2). Then, injections of 2 mL of 1% lidocaine with steroid (a total of 5 mg dexamethasone) and 1500 IU of hyaluronidase were performed separately at each target site. At the end of the procedure, a Racz catheter was retained at the main target site. The catheter was fixed with bio-occlusive dressing. In the recovery room, a test injection of 2 mL of lidocaine was administered through the Racz

catheter. After 10–15 minutes of monitoring, another 4 mL of 10% hypertonic saline was injected through the Racz catheter. The Racz catheter was maintained in place for a 2-day drug-injection regimen. The catheter was removed on the second day after the procedure after the same drugs (2 mL of 1% lidocaine, a total of 5 mg dexamethasone, and 4 mL of 10% hypertonic saline) were injected. Administration of the drug on the second day was performed on an outpatient basis and the patient was discharged after confirming that there was no complication.

Outcome Assessments and Follow-Up

The baseline characteristics of all study patients were collected. Outcome assessments were performed at baseline and at 1, 3, and 6 months after the procedure. Before the procedure, all patients were taught to use the NRS-11 (0 = no pain and 10 = worst possible pain) to assess intensity of both leg and lower back pain (20,21), along with the Korean version of the Oswestry Disability Index (ODI) questionnaire (10-items, range 0–100; 0 = no disability) to assess physical function (22,23). Additionally, the Beck Depression Inventory was used to assess emotional functioning (21) and the Global Perceived Effect of Satisfaction (GPES) was used to assess patient satisfaction and improvement on a 7-point Likert scale (24). The Medication Quantification Scale III (MQS) was also measured to quantify changes in analgesics (25). Adverse events during treatment and follow-up were recorded. A multidimensional approach was used to define these study outcomes.

The primary outcomes were mean differences from baseline pain as measured by the NRS-11 at 1, 3, and 6 months. Secondary outcomes were changes in ODI, MQS, GPES with treatment, and incidence of adverse events in each group during follow-up. Determination of a successful response was based on prior studies with some modifications (17,21,26-28). Successful response was defined as follows: (1) ≥ 50% (or ≥ 4 points) reduction from baseline leg or lower back NRS-11, no increase from baseline ODI and MQS, and ≥ 4 points on the GPES scale; or (2) ≥ 30% (or ≥ 2 points) reduction from baseline NRS-11 with any one of the following criteria: simultaneous ≥ 30% (or ≥ 10 point) reduction in ODI from baseline, ≥ 6 points on the GPES scale, or ≥ 25% reduction from baseline MQS. In addition, NRS-11, ODI, MQS, and GPES scores were determined at 1, 3, and 6 months after the procedure. The changes from baseline for pain intensity, ODI, and MQS were determined at each follow-up assessment. If procedure-related complications were reported, they were recorded, and any adverse events were further evaluated at follow-up visits.

The patients were advised to continue their formerly prescribed analgesic medications. For the first month after the procedure, the patients were instructed not to change any formerly prescribed medications. All patients were aware of this guideline before study participation. The prescribed doses of each analgesic were increased or decreased according to the patient's remnant pain intensity at each follow-up visit. Patients with alterations in analgesic medication were considered as treatment failures after that follow-up visit and were dropped from the study. Patients lost to follow-up, prescribed an increased dose of opioid, or treated surgically or with another procedure were also determined to be treatment failures at that point. Each case of treatment failure was defined as a non-responder at the next follow-up visit.

Sample Size

The study population size was determined on the basis of previous publications (17,29). Assuming a type I error of .05 (2-tailed) and a power of .80, a minimum of 20 patients per group was required for between-group comparisons. Because the drop-out rate was 30% at 6 months in a previous study (17), we decided to enroll 30 patients.

Statistical Analysis

Categorical variables are presented as absolute numbers and percentages. Continuous variables are presented as means with standard deviation, 95% confidence intervals, or medians with interquartile range. To compare data between groups, the χ^2 test or Fisher's exact test were used to assess categorical variables and the Student's t test or Mann–Whitney U-test were used to analyze continuous variables, as appropriate. All observed data were analyzed on an intent-to-treat (ITT) basis, regardless of loss to follow-up or dropout from the study. Because data loss resulting from dropout, including treatment failure, was expected, a linear mixed-effect model was used to analyze continuous variables (NRS-11, ODI, MQS, and GPES) at baseline and 1, 3, and 6 months after the procedure. For strict interpretation of the results of this study, successful follower analysis was performed with consideration of all follow-up losses as treatment failures. All data manipulations and statistical analyses were performed using SPSS Version 21 (IBM Corporation, Armonk, NY) and Stata Version

13.1 (StataCorp LP, College Station, TX). A 2-tailed *P* value of < .05 was considered to indicate a statistically significant difference.

Results

Between January 2014 and June 2016, a series of 604 patients diagnosed with LSS were screened for eligibility to participate in the study. These patients presented with chronic lower back pain with or without lumbar radicular pain. A total of 60 patients who fulfilled both the inclusion and exclusion criteria agreed to participate in this study. After randomization, 30 patients each were assigned to the Racz (balloon-less) and the ZiNeu (inflatable balloon) groups. Among the 30 eligible Racz group patients, 10 patients did not receive the allocated intervention or did not visit again, and one patient experienced a complication (suspicious dura mater puncture). Among the 30 eligible ZiNeu group patients, 6 did not receive the allocated intervention or did not visit again, and one patient experienced a complication (suspicious dura mater puncture). Thus, a total of 44 patients (20 in the Racz group and 24 in the ZiNeu group) were included in the ITT analysis. All 44 patients underwent follow-up at 1, 3, and 6 months. By the 3-month follow-up examinations, 3 patients (15.0%) in the Racz group and 2 patients (8.3%) in the ZiNeu group had dropped out. At the last follow-up examination at 6 months, a total of 5 patients in each group had dropped out. At study completion, 15 patients (75.0%) in the Racz group and 19 patients (79.2%) in the ZiNeu group were still enrolled (Fig. 3). The reason for dropout was that the patient had undergone another procedure during follow-up or had not visited again.

As indicated in Table 1, groups were not significantly different in baseline demographic characteristics except for diabetes as a concurrent disease and total duration of pain ($P < .03$). The estimated mean changes in pain (NRS-11) and functional status (ODI) from baseline over the 6-month follow-up are shown in Table 2 and Fig. 4. The results of these ITT analyses showed that the pain intensities of the lower back and leg and the functional capacity of both groups were improved from baseline at 3 months following PEA. These effects (back and leg pain and ODI) of treatment were maintained at 6 months in the ZiNeu group, but not in the Racz group. In addition, according to the responder analysis, the proportion of successful responders was higher in the ZiNeu group than in the Racz group throughout the follow-up (Table 3). Furthermore, there was a statistically significant difference between groups at 6 months after PEA ($P = .035$).

Table 4 shows the observed numbers of patients who satisfied the individual criteria of a successful response at each follow-up visit. There was a significant difference between groups in NRS-11 reduction ≥ 50% (or 4 points), ODI reduction ≥ 30% (or 10 points), GPES ≥ 6 and ≥ 4 points at 6 months, and NRS-11 reduction ≥ 50% (or 4 points) at 3 months after PEA ($P < .03$). However, MQS was not significantly different between groups. GPES in the ZiNeu group was higher than in the Racz group (Table 5), demonstrating statistically significant differences at 3 and 6 months after PEA ($P = .039$ and $P = .014$, respectively).

Serious adverse events were not observed in any study patients, and minor adverse events that presented during the study period were transient. Some patients complained of 2–3 days of pain after PEA, but temporary pain aggravation was relieved spontaneously without any neurological sequelae in all cases. Some patients reported transient pain during needle insertion and paresthesia during adhesiolysis, which was bearable and did not require extra medication or termination of PEA. No other complications or adverse events, such as intravenous injection, severe pain or paresthesia, persistent motor or sensory impairment, or infection, were reported except for suspicious dura mater puncture. No withdrawal from the study because of adverse effects was noted.

Discussion

LSS functional disability, such as neurogenic claudication, is one of the most common causes of chronic lower back and leg pain in aged people (2,3). PEA, which can relieve adhesion, has recently been recommended for patients with severe LSS who fail to respond to conventional treatment, including ESI (4,9,13). However, there has been no study comparing the effects of PEA combined with ballooning and conventional PEA with a Racz catheter. The objective of this study was to compare the treatment response between combined PEA with balloon decompression and PEA only in patients with central LSS. The present study is the first randomized controlled trial showing the clinical efficacy of a newly developed ZiNeu catheter for patients with central LSS.

We set the minimally important change to 2 points or 30% in the NRS-11 pain scores and 10 points or 30% in the ODI. We found that, for patients who were refractory to conventional ESI, PEA using a ZiNeu

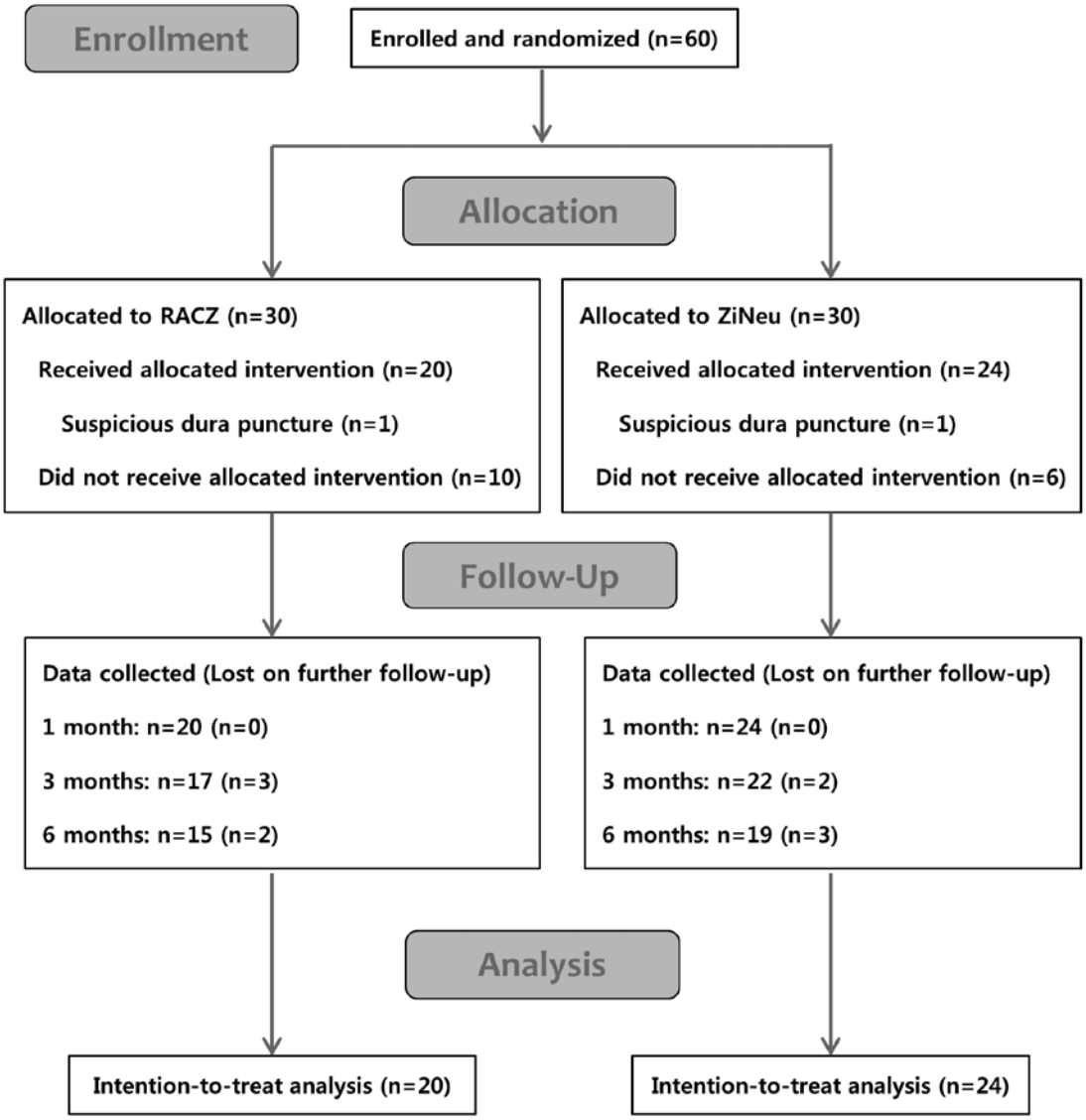

Fig. 3. *CONSORT flow diagram of patients in this trial. Sixty patients were randomly assigned to the Racz (n = 30) or ZiNeu (n = 30) groups. At 6 months after the procedure, 20 and 24 patients remained in each arm, respectively.*

catheter provided better pain relief and maintenance of that relief for 6 months after the procedure than did PEA using the Racz catheter. These patients also experienced significant functional improvement after the procedure, as shown by improved ODI scores. Our results suggest that PEA using a ZiNeu catheter may have beneficial effects for refractory central LSS patients with functional impairment and neurogenic claudication. In addition, the ZiNeu group patients showed higher satisfaction with the procedure for 6 months compared to the Racz group patients. The percentage of successful responders at 6 months, as measured by various indicators including the NRS-11, ODI, GPES, and MQS, was higher in the ZiNeu group than in the Racz

Table 1. *Baseline characteristics of each group*

Parameters	Racz (n = 20)	ZiNeu (n = 24)	*P* Value
Age (yrs)	66.1 ± 12.2	65.5 ± 6.4	.834
Gender (men / women)	9 (45.0%) / 11 (55.0%)	17 (70.8%) / 7 (29.2%)	.125
Body mass index (kg/m2)	24.3 ± 2.4	24.3 ± 2.2	.959
Concurrent disease Diabetes Hypertension CV CVA Other	 1 (5.0%) 8 (40.0%) 3 (15.0%) 0 (0%) 3 (15.0%)	 8 (33.3%) 7 (29.2%) 2 (8.3%) 2 (8.3%) 3 (12.5%)	 .027 .450 .646 .493 .810
Spondylolisthesis	3 (15.0%)	6 (25.0%)	.477
Neuropathic component	6 (30.0%)	5 (20.8%)	.484
Total duration of pain (mos)	17.0 ± 15.5	59.5 ± 84.5	.023
Number of previous epidural injections	3.3 ± 2.8	3.7 ± 3.5	.616
Previous epidural adhesiolysis	3 (15.0%)	3 (12.5%)	.810
Medication Quantification Scale	4.0 (0–8.2)	4.0 (0–8.0)	.532
Opioid use	2 (10.0%)	1 (4.2%)	.583
Central stenosis grades Mild Moderate Severe	0 (0%) 5 (25.0%) 15 (75.0%)	0 (0%) 3 (12.5%) 21 (87.5%)	1.000 .436 .436
Target level One Two Three	16 (80.0%) 3 (15.0%) 1 (5.0%)	20 (83.3%) 4 (16.7%) 0 (0%)	.775 .880 .455
Pain intensity (Numerical Rating Scale) Leg Back	7.0 (4.0–8.0) 7.0 (6.0–8.0)	6.0 (6.0–8.0) 6.0 (3.0–8.0)	.646 .311
Oswestry Disability Index (%)	41.3 ± 14.3	37.7 ± 12.4	.372
Beck Depression Inventory	12.0 (4.0–24.0)	7.0 (2.0–10.5)	.057

Data are expressed numbers (%), means ± standard deviation, or medians (interquartile range). CV = cardiovascular disease; CVA = cardiovascular accident; Other = malignancy, osteoarthritis of knee, osteoporosis, benign prostate hyperplasia, liver disease, respiratory disease, or Parkinson's disease.

Table 2. *Changes in adjusted predictions of pain scores and physical function after percutaneous epidural adhesiolysis using balloonless (Racz) or inflatable balloon (ZiNeu) catheter in intractable lumbar central canal stenosis patients.*

Variables	Time	Adjusted Prediction (95% CI)		Estimated Difference (95% CI)*	*P* Value
		Racz	ZiNeu		
Back pain (NRS-11)	Baseline	6.45 (5.39–7.51)	5.50 (4.53–6.47)	−0.95 (−2.39–0.49)	.195
	1 mo	4.25 (3.19–5.31)	3.88 (2.91–4.84)	−0.38 (−1.81–1.06)	.609
	3 mos	4.54 (3.40–5.67)	3.41 (2.42–4.40)	−1.13 (−2.63–0.38)	.142
	6 mos	5.00 (3.80–6.15)	2.96 (1.92–3.99)	−2.02 (−3.58–−0.45)	.011
Leg pain (NRS-11)	Baseline	6.30 (5.47–7.13)	6.71 (5.95–7.47)	0.41 (−0.71–1.53)	.476
	1 mo	4.15 (3.32–4.98)	4.88 (4.12–5.63)	0.73 (−0.40–1.85)	.206
	3 mos	4.71 (3.80–5.62)	4.02 (3.24–4.81)	−0.69 (−1.89–0.52)	.263
	6 mos	5.46 (4.50–6.42)	3.58 (2.75–4.41)	−1.88 (−3.15–−0.61)	.004
ODI (%)	Baseline	41.30 (35.58–47.02)	37.67 (32.44–42.89)	−3.63 (−11.38–4.11)	.358
	1 mo	32.80 (27.08–38.52)	26.67 (21.44–31.89)	−6.13 (−13.88–1.61)	.121
	3 mos	31.85 (25.75–37.95)	25.22 (19.86–30.57)	−6.63 (−14.75–1.48)	.109
	6 mos	35.62 (29.28–41.96)	21.89 (16.31–27.46)	−13.74 (−22.18–−5.30)	.001

A numerical rating scale (NRS-11) was used to assess the intensity of both lower back and leg pain. The Oswestry Disability Index (ODI) was used to assess physical function. A linear mixed model was used for the statistical analysis. *Estimated difference in values between groups. *P* values for interactions between group and time for back pain, leg pain, and ODI = .156, .001, and .074, respectively. CI = confidence interval.

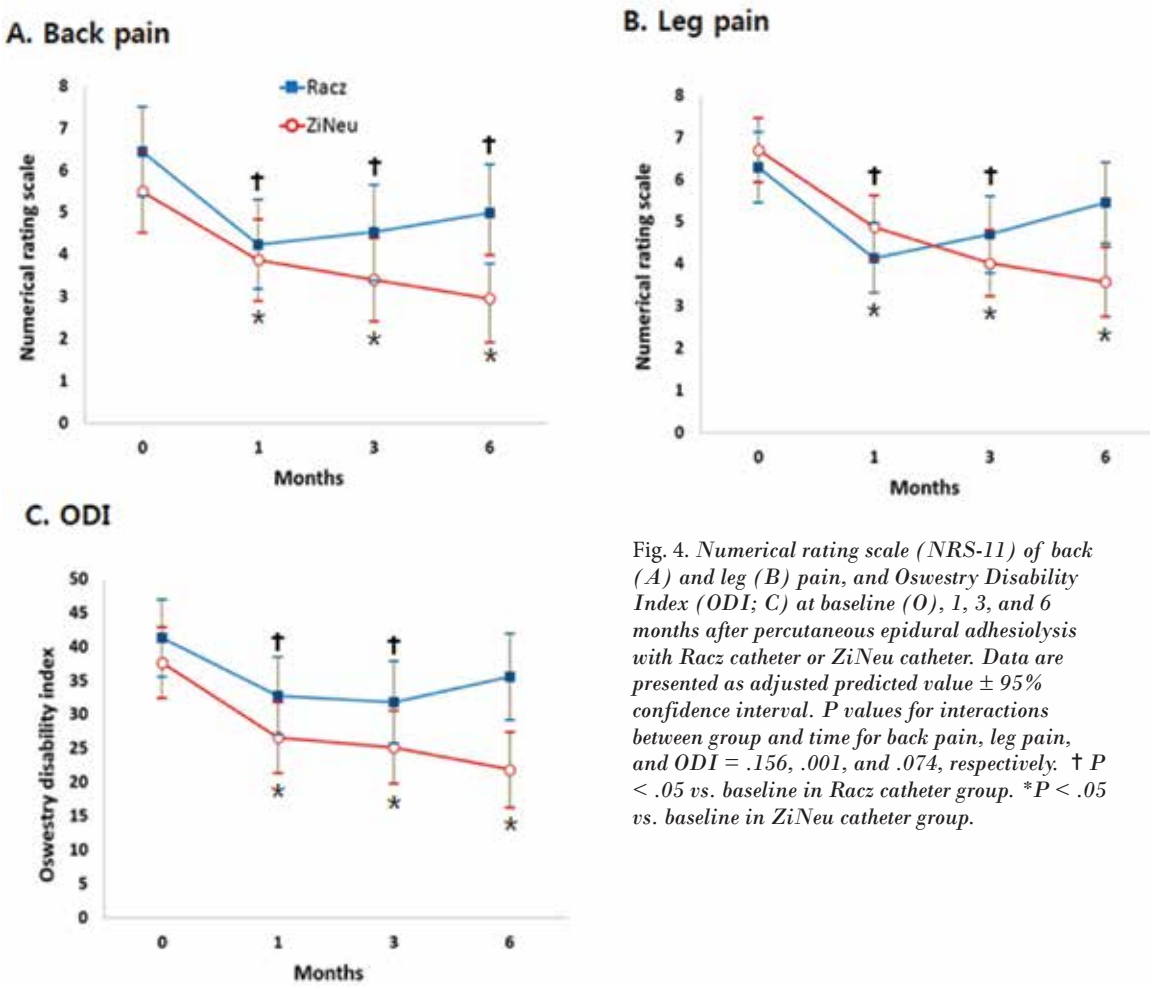

Fig. 4. *Numerical rating scale (NRS-11) of back (A) and leg (B) pain, and Oswestry Disability Index (ODI; C) at baseline (0), 1, 3, and 6 months after percutaneous epidural adhesiolysis with Racz catheter or ZiNeu catheter. Data are presented as adjusted predicted value ± 95% confidence interval. P values for interactions between group and time for back pain, leg pain, and ODI = .156, .001, and .074, respectively.* † *P < .05 vs. baseline in Racz catheter group.* **P < .05 vs. baseline in ZiNeu catheter group.*

Table 3. *Proportions of successful responders among the intractable lumbar central canal stenosis patients treated using balloon-less (Racz) or inflatable balloon (ZiNeu) catheter*

Parameters	Follow-up	Racz (n = 20)	ZiNeu (n = 24)	*P* Value
Successful responders	1 mo	8 (40.0%)	14 (58.3%)	.364
	3 mos	8 (40.0%)	14 (58.3%)	.364
	6 mos	5 (25.0%)	14 (58.3%)	.035

Successful response was defined as follows: (1) ≥ 50% (or ≥ 4-point) reduction from baseline leg or lower back NRS-11, and no increase from baseline ODI and MQS, and ≥ 4 points on the GPES scale or (2) ≥ 30% (or ≥ 2-point) reduction from baseline NRS with any one of the following criteria: simultaneous ≥ 30% (or ≥ 10-point) reduction in ODI from baseline, ≥ 6 points on the GPES scale, or ≥ 25% reduction in MQS from baseline. Data are expressed as numbers (%). Racz = intractable lumbar central canal stenosis patients treated with percutaneous epidural adhesiolysis using balloon-less Racz catheter. ZiNeu = intractable lumbar central canal stenosis patients treated with combined epidural adhesiolysis and balloon decompression using an inflatable balloon ZiNeu catheter.

group. In our study, the ZiNeu group showed superior improvements in lower back and/or leg pain, ODI, and GPES than the Racz group at all assessment points after the procedure, although there was no significant difference between groups in the decrease in MQS scores.

This present study is unique given the comparison of PEA with an inflatable balloon catheter to a balloon-less catheter in patients with central LSS. Several factors

Table 4. *Observed number of patients who satisfied the individual parameters for a successful response at each follow-up visit.*

Parameters	Follow-up	Racz (n = 20)	ZiNeu (n = 24)	*P* Value
≥ 50% (or ≥ 4 points) reduction in NRS-11	1 mo	6 (30.0%)	10 (41.7%)	.534
	3 mos	3 (15.0%)	12 (50.0%)	.025
	6 mos	1 (5.0%)	13 (54.2%)	.001
≥ 30% (or ≥ 2 points) reduction in NRS-11	1 mo	11 (55.0%)	16 (66.7%)	.429
	3 mos	8 (40.0%)	16 (66.7%)	.128
	6 mos	8 (40.0%)	15 (62.5%)	.225
≥ 30% (or ≥ 10 points) reduction in ODI	1 mo	6 (30.0%)	13 (54.2%)	.135
	3 mos	7 (35.0%)	15 (62.5%)	.129
	6 mos	4 (20.0%)	13 (54.2%)	.030
No increase from baseline ODI	1 mo	17 (85.0%)	21 (87.5%)	.810
	3 mos	16 (80.0%)	20 (83.3%)	.775
	6 mos	15 (75.0%)	21 (87.5%)	.436
≥ 6 points in GPES	1 mo	6 (30.0%)	10 (41.7%)	.534
	3 mos	4 (20.0%)	12 (50.0%)	.060
	6 mos	3 (15.0%)	12 (50.0%)	.025
≥ 4 points in GPES	1 mo	12 (60.0%)	20 (83.3%)	.102
	3 mos	12 (60.0%)	21 (87.5%)	.078
	6 mos	10 (50.0%)	20 (83.3%)	.025
≥ 25% reduction in MQS	1 mo	3 (15.0%)	3 (12.5%)	.810
	3 mos	3 (15.0%)	4 (16.7%)	1.000
	6 mos	3 (15.0%)	3 (12.5%)	.810
No increase from baseline MQS	1 mo	13 (65.0%)	13 (54.2%)	.547
	3 mos	12 (60.0%)	10 (41.7%)	.364
	6 mos	10 (50.0%)	8 (33.3%)	.359

Data are expressed as numbers (%). NRS-11 = Numerical Rating Scale; ODI = Oswestry Disability Index; GPES = Global Perceived Effect of Satisfaction; MQS = Medication Quantification Scale. Racz = intractable lumbar central canal stenosis patients treated with percutaneous epidural adhesiolysis using balloon-less Racz catheter. ZiNeu = intractable lumbar central canal stenosis patients treated with combined epidural adhesiolysis and balloon decompression using an inflatable balloon ZiNeu catheter.

Table 5. Changes in the Global Perceived Effect of Satisfaction in 2 groups.

Parameters	Follow-up	Racz (95% CI) *	ZiNeu (95% CI) *	*P* Value
GPES	1 mo	4.44 (3.86–5.74)	5.00 (4.60–5.78)	.258
	3 mos	4.35 (3.70–5.37)	5.36 (4.73–6.03)	.039
	6 mos	4.20 (3.50–4.90)	5.33 (4.73–5.93)	.014

Data are expressed as mean (95% CI). *Mean values were calculated using a linear mixed model. GPES = Global Perceived Effect of Satisfaction, CI = confidence interval.

could have contributed to functional improvement, effective pain relief, and higher satisfaction after PEA with an inflatable balloon catheter compared to a balloon-less catheter. First, the inflatable balloon catheter is more capable of reaching difficult target sites because it is thicker and easier to manipulate. The ZiNeu catheter can be manipulated both side-to-side and vertically (17). Although there may be concern about adverse effects such as nerve damage and dura mater tear because of the thicker catheter or balloon inflation/deflation, previous studies have shown that there is no sustained and severe adverse effect (16,17,30). In addition, there was no difference in adverse events between groups in the current study. Second, after approaching the target point of central LSS, the spread of drugs, such as local anesthetics and steroids, would be facilitated if the adhesion is relieved by balloon inflation. Balloon inflation would allow for more effective distribution of epidural injections to the involved region of central LSS. The distribution of the drug would contribute to more effective decreases in

neurogenic and perineural inflammation. Third, expansion of the epidural space by balloon inflation would be effective for mechanical disentanglement of perineural adhesions, which would play a role in decreasing long-lasting pain and improving function. Adhesion and fibrosis in the epidural space would develop because of inflammation around the involved neural tissue (31), and such factors interfere with the motility of nerve roots and cause radiculopathy (32). Lastly, mechanical balloon inflation/deflation would lead to decreased mechanical irritation and venous congestion at the target site. Venous congestion is known to be an essential factor inducing neurogenic recurrent claudication and precipitating circulatory disturbance in compressed nerve roots (33,34). Perineural fibrosis associated with venous congestion may interfere with nutrient transfer and cause predisposition to nerve stretch injury (35).

Although several studies have shown that conventional PEA is effective for treating epidural adhesion of patients with LSS (8-11,36), there are limitations, such as weakness and short duration of treatment effect. Our study shows that PEA using an inflatable balloon catheter has a superior therapeutic effect and duration than PEA using a balloon-less catheter. Even in the ZiNeu group, NRS-11 and ODI scores decreased over 6 months, whereas the Racz group decreased over one month, but the effect diminished after one month. This is probably because of balloon inflation/deflation and the resulting increase in the diameter of the epidural space. In a previous study, Kim et al demonstrated the effect of the balloon, which increased the diameter of the epidural space by 10.5%–31.8% (median 28.0%) (30). This ballooning effect supports the therapeutic mechanism of PEA using the ZiNeu catheter and provides evidence of successful epidural space expansion. In contrast, adhesiolysis performed with the Racz catheter is based on the concept of chemical adhesiolysis through the administration of a drug to the target site (i.e., saline flushing); this resolves filling defects rather than providing mechanical adhesiolysis. Combining epidural PEA and balloon decompression results in mechanical adhesiolysis through the ballooning procedure and chemical adhesiolysis through drug administration at the same time. The ZiNeu catheter procedure differs from adhesiolysis with a Racz catheter in that the ZiNeu catheter is placed in either the ventral or dorsal epidural space; whereas, the Racz catheter is usually placed in the ventral lateral epidural space, with midline positioning to be avoided. Success with PEA without a balloon has been shown to be related to foraminal filling with dye, but not with the extent of stenosis. PEA without a balloon is also accompanied by postprocedural exercises called neural flossing.

This study has several limitations. First, the application of the present results may be limited to central stenosis, although the ballooning procedure can be helpful for foraminal stenosis (30). We are currently performing a multicenter prospective investigation of PEA using the ZiNeu catheter performed in patients with both foraminal and central stenosis. Second, the results may vary according to the definition of successful response. We cautiously designated response criteria to reflect the success of the procedure as either substantial or clinically meaningful pain reduction combined with patient-reported outcomes, including the ODI, MQS, and GPES (20,23,37). Third, the groups differed with regard to prevalence of diabetes and total duration of pain. Despite the fact that the prevalence of diabetes was higher and the total duration of pain longer in the ZiNeu group, the treatment effect was paradoxically better in the ZiNeu group than in the Racz group. Therefore, the difference in the prevalence of diabetes and total duration of pain did not seem to affect the outcome of the 2 groups. Finally, the follow-up loss in the present study seemed to be high. Since this study was performed in one of the largest centers in Korea, a significant proportion of the patients were from different cities. Having a high proportion of patients in remote areas may have influenced the extent of follow-up loss. Therefore, the linear mixed model was used to adjust for missing values and an ITT-based analysis was performed. Furthermore, in order to interpret the results of this study strictly, all follow-up loss was considered as treatment failure in responder analysis.

Conclusion

In conclusion, PEA using the inflatable balloon catheter leads to significant pain reduction and functional improvement in patients with central LSS compared to PEA using the balloon-less catheter. Therefore, we suggest that this can be a useful alternative modality in refractory central LSS patients who have not responded to conventional treatment, including pre-existing PEA using a ball°on-less catheter.

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