Randomized Trial

Comparison of Epidural Spreading Patterns and Clinical Outcomes of Transforaminal Epidural Steroid Injection with High-Volume Injectate via the Subpedicular Versus the Retrodiscal Approach

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Free full manuscript: www.painphysicianjournal.com **Background:** The effect of transforaminal epidural steroid injection (TFESI) appears to be influenced by the volume of the injected material because there is a positive correlation between injection volume and extent of pain relief.

Objectives: The purpose of this study was to examine how many vertebral segments are covered by the subpedicular (SP) approach and the retrodiscal (RD) approach and to compare the clinical outcomes of the 2 approaches in TFESI with high-volume injectates.

Study Design: A randomized, active control trial.

Setting: Medical University centers.

Methods: Fifty patients were randomly assigned to either the SP group or the RD group. TFESI was performed with high-volume injectates. A total of 9 mL injectate was divided into 3 injections (0.5 mL, 2.5 mL, and 6 mL) given at 10-second intervals. The primary outcome measure was injectate distribution. The spreading patterns were described as unilateral, bilateral, ventral, or dorsal. Ventral or dorsal flow was also described as being cephalad or caudad, respectively. The secondary outcome measures were pain relief and reduction of functional disability at 4 weeks after the procedure.

Results: The total numbers of vertebral segments and median levels of contrast spread from the injection site were not significantly different between the 2 groups. However, in 3 mL of injectate, the injectate spread showed more extensive bilateral distribution in the RD group. At 4 weeks after treatment, both groups demonstrated statistically significant pain relief and improvement in functional status. No significant differences were observed between the 2 groups.

Limitations: We enrolled only a small number of patients and did not analyze long-term outcomes. Patients with severe spinal stenosis or herniated nucleus pulposus were included. Slightly different methods were used in the 2 groups to determine the number of levels at which the injectate was spread.

Conclusions: Epidural spreading patterns and clinical outcomes of lumbar TFESI with high-volume injectate were not significantly different between the SP approach and the RD approach.

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Key words: Epidural injections, epidural space, low back pain, radiating pain, disability evaluation, steroids, local anesthetics, intervertebral disc disease, spinal stenosis

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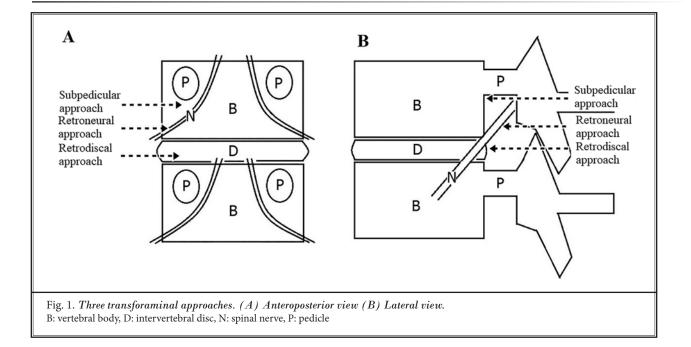
n epidural steroid injection (ESI) procedure can take an interlaminar, caudal, or transforaminal (TF) approach, depending on the particular site at which a needle is inserted into the epidural space. The TF approach is generally preferred because delivery of a therapeutic injectate transforaminally at the involved nerve root maximizes steroid concentration at the site of pathology; moreover, the injectate can be delivered to the anterior epidural space of the symptom-associated nerve root (1,2).

Several mechanisms have been suggested to explain the anti-inflammatory action of epidural corticosteroids on lumbosacral radiculopathy (3,4). These corticosteroids can inhibit the production of arachidonic acid or the occurrence of ectopic discharge from unmyelinated C-fibers. Alternatively, they can relieve central sensitization (5,6). The effect of TFESI might be influenced by the volume of the injected material. A positive correlation has been reported between fluid injection volume into the epidural space and relief of radicular leg pain and low back pain (7). The injected material displaces the dura forward and inward, in addition to stretching the nerve roots. These effects lead to lysis of neural adhesions (7).

The TF approach can be divided into 3 approaches – the subpedicular (SP) approach, the retroneural (RN) approach, and the retrodiscal (RD) approach – depending on where the needle is advanced (Fig. 1). The SP ap-

proach is currently used most frequently in clinical practice. In this approach, an injection needle is advanced into the safe triangle under the inferior aspect of the pedicle, as described by Bogduk (8). Two alternative approaches for TFESI include the RN approach and the RD approach. The RN approach has an optimal target area more dorsal to the intervertebral foramen compared with the SP approach (9). In the RD approach, the needle is advanced into the inferior aspect of the foramen (10). This technique has the advantage that the injection can be made closest to the nerve root, which is stimulated by a prolapsed intervertebral disc (IVD). However, it is not clear which TFESI method is preferred for treatment of lumbar radiculopathy. Some studies have concluded that TFESI for lumbar radiculopathy with the RD approach is more effective than TFESI with the SP approach (11), but others have reached different conclusions (12).

To the best of our knowledge, no controlled trials have examined the epidural spreading patterns or clinical outcomes of a high-volume injectate via the SP approach versus the RD approach in patients undergoing lumbar TFESI. The purpose of this study was therefore to determine how many spinal segments are covered by the two approaches and to compare the clinical effects of delivering a high-volume injectate (with the same dose of dexamethasone) by the 2 approaches.



METHODS

This randomized, active control trial study was conducted with the full approval of the Institutional Review Board of Ewha Womans University Hospital (EUMC 2015-05-003-003) and in accordance with the ethical principles of the Declaration of Helsinki. An informed consent was presented to all patients prior to enrollment in the study groups. Written informed consent to participate were obtained from all the patients.

Randomization

Fifty patients were enrolled and randomly assigned to either the SP group or the RD group. The random numbers were kept in a sealed location and were opened by an anesthesiologist uninvolved in this study.

Patients

The inclusion criteria were A) presence of lumbar radiculopathy with a pain intensity $\geq 40/100$ in a patient diagnosed with a herniated nucleus pulposus (HNP) or spinal stenosis (SS) after a series of physical, neurologic, and radiologic examinations; B) one-level TFESI from L3 to L5; C) no prior therapeutic TFESI within the previous 6 months; and D) no prior surgery. The exclusion criteria were A) long-term oral steroid treatment, B) pregnancy, C) cognitive impairment, and D) use of any anti-coagulant.

Outcome Measures

The primary outcome measure for this study was injectate distribution. To examine the injection distribution pattern, the spread was confirmed using fluoroscopic images (anteroposterior and lateral view), and the maximum distribution was determined. The spreading pattern in each patient was analyzed by a single experienced pain physician and a single experienced radiologist, neither of whom was involved in the procedure. If the 2 physicians did not agree on the results of the analysis, an additional experienced pain physician assessed the fluoroscopic images, and a consensus was reached. The spreading patterns were described as unilateral, bilateral, ventral, or dorsal. Ventral or dorsal flow was also described as being cephalad or caudad, respectively. In the SP group, the flow level was defined as being from the pedicle at the injection site to the cephalad or caudad pedicle (13). Thus, if an injection was performed at the L4 level and the injectates reached the L3 pedicle, the injection would be recorded as one level of cephalad flow. If the injectates reached the L5 pedicle, the injection would be recorded as one level of caudad flow (Fig. 2A). In the RD group, the flow level was defined as being from the IVD at the site of injection to the cephalad or caudad IVD (the superior aspect of the adjacent superior

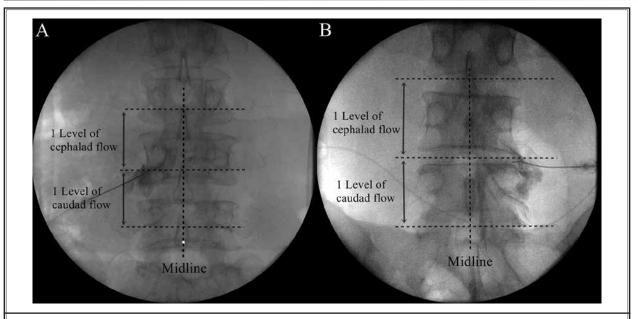


Fig. 3. Levels of epidural spreading. (A) Anteroposterior view of the subpedicular approach at the L4/5 intervertebral level. Note the inferior aspect of the adjacent superior pedicle and the inferior aspect of the adjacent inferior pedicle. (B) Anteroposterior view of the retrodiscal approach at the L4/5 intervertebral level. Note the superior aspect of the adjacent superior IVD and the inferior aspect of the adjacent inferior IVD.

IVD and the inferior aspect of the adjacent inferior IVD, respectively) (14). Thus, if an injection was performed at the L4/5 IVD and the injectates reached the L3/4 IVD, the injection would be recorded as one level of cephalad flow. If the injectates reached the L5/S1 IVD, the injection would be recorded as one level of caudad flow (Fig. 2B).

The secondary outcome measures were pain relief and reduction of functional disability at 4 weeks after the procedure. Pain relief was assessed using the Visual Analog Scale (VAS, range 0 – 100). Reduction of functional disability was evaluated by the Korean version of the Roland-Morris Disability Questionnaire (RMDQ, range 0 – 24) (15). All complications and side effects were recorded.

Procedures

All of the TFESIs were performed in a procedure suite at an ambulatory surgery center. The first author was present for all procedures performed. We performed TFESI with high-volume injectates (9 mL total; 0.33% lidocaine with 5 mg of dexamethasone mixed with 5 mL of contrast medium) in both groups. A total of 9 mL injectate was given in 3 injections (0.5 mL, 2.5 mL, and 6 mL) at 10-second intervals. The injectate was introduced under real-time continuous fluoroscopy at a consistent rate of 0.5 to 1.0 mL/sec and monitored manually.

Each patient was placed in the prone position with a pillow under the lower abdomen and above the iliac crest to reduce lumbar lordosis, prepared for the injection, and draped using a sterile technique. The cephalo-caudal angle of the C-arm was adjusted, allowing the incident x-ray beam to be parallel to the inferior and superior end plates of the IVD. Vital signs were monitored.

In the SP group, the right and left angles of the C-arm were rotated toward the lesion site by 15-25 degrees. A 22-gauge, 5-inch spinal needle was guided inferior to the pars interarticularis and into the intervertebral foramen. With the use of biplanar visualization, the needle was advanced into the "safe triangle," which was inferior to the pedicle and superolateral to the exiting spinal nerve. In the lateral projection, needle placement was confirmed with the needle tip approximately 1 to 2 mm dorsal to the posterolateral vertebral body.

In the RD group, the right and left angles of the C-arm were rotated toward the lesion site by 40-50 degrees so that the superior articular process was po-

sitioned and visible in the middle of the IVD. At this position, a 22-gauge, 5-inch spinal needle was directed to the middle of the IVD, using the lateral aspect of the superior articular process. The needle was advanced until the tip reached the outer wall of the annulus fibrosus. In this process, special care was taken to ensure that the needle did not penetrate the annulus fibrosus of the IVD, with particular attention given to the anteroposterior and the lateral C-arm images.

Statistical Aanalysis

To calculate the required sample size, data from our previous study were taken into consideration (16). A total of 50 patients were determined to be required to detect a 30% decrease in the VAS score between the groups with a power of 0.8 and α equal to 0.05.

The normal distribution of continuous variables was evaluated by the Shapiro-Wilk test. Parametric data were analyzed using the independent t-test, while non-parametric data were analyzed with the Mann-Whitney U-test and the Wilcoxon signed-rank test. Descriptive variables were evaluated by the χ 2 test. Continuous variables are expressed as mean \pm standard deviation, whereas ordinal data and nonparametric data are expressed as median (interquartile range; P25 - P75) or number. The degree of agreement among observers was expressed using Kappa values with confidence intervals.

P-values<0.05 were considered statistically significant. All statistical analyses were performed using SPSS 18 software (Chicago, IL, USA) except for Kappa values, which were obtained using SAS software version 9.1 (SAS Institute, Cary, NC).

RESULTS

The 50 patients who visited the pain clinic were randomized into equal groups of 25 patients each. In the SP group, 2 patients were lost to follow-up. Consequently, 23 patients remained in the SP group, and 25 were present in the RD group (Fig. 3). There were no significant differences between the 2 groups in demographic data (Table 1).

Primary Outcomes

All patients demonstrated ventral epidural spread. The total numbers of vertebral segments marked by injectate spread were not significantly different between the 2 groups. However, in 3 mL of injectate, the injectate spread showed a statistically significantly (P = 0.04) stronger bilateral distribution in the RD group (Table 2).

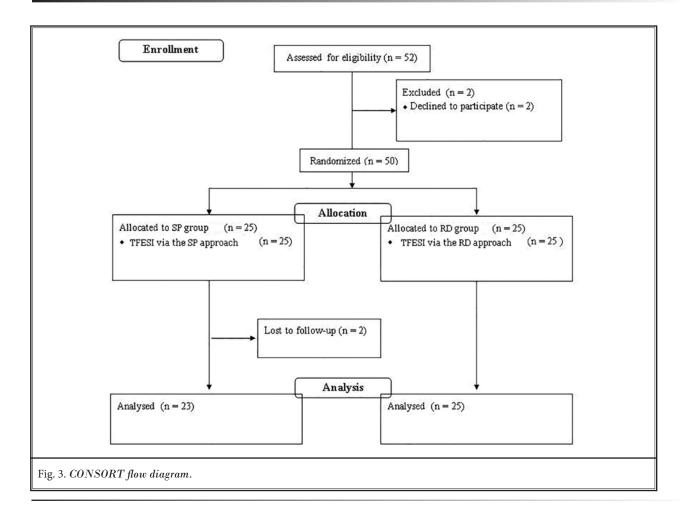


Table 1. Demographic data

	SP Group (n = 23)	RD Group (n = 25)	P-value			
Age (y)	60.3 ± 13.7	57.2 ± 13.8	0.43			
Sex (M/F)	8 / 15	14 / 11	0.14			
Height (cm)	160.2 ± 9.2	163.4 ± 11.2	0.28			
Weight (kg)	62.3 ± 10.6	63.6 ± 11.3	0.68			
Levels injected (L3/L4/L5)	3 / 13 / 7	1 / 21 / 3	0.11			
Injection site (Left / Right)	11 / 12	12 / 13	0.99			
Radiologic findings						
Central stenosis	10	12	0.75			
Foraminal stenosis	9	6	0.26			
L3/4 HNP	8	3	0.06			
L4/5 HNP	14	16	0.82			
L5/S1 HNP	4	3	0.59			

Data are expressed as mean \pm standard deviation or number. HNP: herniated nucleus pulposus

		SP Group (n = 23)	RD Group (n = 25)	P-value
Number of	patients			
0.5 mL	Unilateral / Bilateral	23 / 0	25 / 0	> 0.99
	Level of ventral cephalad flow (0 / 1 / 2 / 3)	23 / 0 / 0 / 0	22 / 3 / 0 / 0	0.08
	Level of ventral caudad flow (0 / 1 / 2 / 3)	23 / 0 / 0 / 0	25 / 0 / 0 / 0	> 0.99
	Level of dorsal cephalad flow (0 / 1 / 2 / 3)	23 / 0 / 0 / 0	25 / 0 / 0 / 0	> 0.99
	Level of dorsal caudad flow (0 / 1 / 2 / 3)	23 / 0 / 0 / 0	24 / 1 / 0 / 0	0.33
2.5 mL	Unilateral / Bilateral	21 / 2	17 / 8	0.04
	Level of ventral cephalad flow (0 / 1 / 2 / 3)	5 / 14 / 3 / 1	5 / 14 / 6 / 0	0.58
	Level of ventral caudad flow (0 / 1 / 2 / 3)	14/9/0/0	12 / 13 / 0 / 0	0.37
	Level of dorsal cephalad flow (0 / 1 / 2 / 3)	12/9/1/1	14 / 11 / 0 / 0	0.51
	Level of dorsal caudad flow (0 / 1 / 2 / 3)	12 / 11 / 0 / 0	18 / 7 / 0 / 0	0.16
6 mL	Unilateral / Bilateral	11 / 12	11 / 14	0.79
	Level of ventral cephalad flow (0 / 1 / 2 / 3)	4/6/6/7	1 / 6 / 10 / 8	0.59
	Level of ventral caudad flow (0 / 1 / 2 / 3)	5/16/2/0	8 / 12 / 5 / 0	0.29
	Level of dorsal cephalad flow (0 / 1 / 2 / 3)	7/7/3/6	8 / 5 / 8 / 4	0.39
	Level of dorsal caudad flow (0 / 1 / 2 / 3)	5/15/3/0	11 / 10 / 4 / 0	0.19
Median leve	els of contrast spread from injection site			
0.5 mL	Ventral cephalad flow	0 (0)	0 (0)	0.09
	Ventral caudad flow	0 (0)	0 (0)	> 0.99
	Dorsal cephalad flow	0 (0)	0 (0)	> 0.99
	Dorsal caudad flow	0 (0)	0 (0)	0.34
2.5 mL	Ventral cephalad flow	1 (0)	1 (0.5)	0.71
	Ventral caudad flow	0 (1.0)	1 (1.0)	0.38
	Dorsal cephalad flow	0 (1.0)	0 (1.0)	0.60
	Dorsal caudad flow	0 (1.0)	0 (1.0)	0.16
6 mL	Ventral cephalad flow	2 (2.0)	2 (2.0)	0.37
	Ventral caudad flow	1 (0)	1 (1.0)	0.97
	Dorsal cephalad flow	1 (3.0)	1 (2.0)	0.95
	Dorsal caudad flow	1 (2.0)	1 (1.0)	0.26

Table 2. Epidural spreading patterns

Data are expressed as median (interquartile range; P25 - P75) or number.

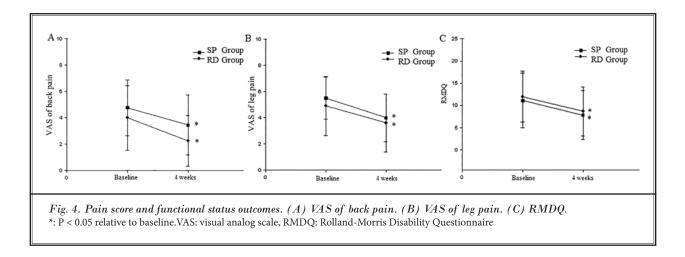
The Kappa value range (95% confidence interval) was 0.7895 (0.3903 - 1) - 1.

Secondary Outcomes

There were no significant differences in baseline VAS score for back and radicular pain or in RMDQ score between the 2 groups. At 4 weeks after treatment, both groups demonstrated statistically significant improvement in back and leg pain according to VAS score and improvement in functional status according to RMDQ score (P < 0.05). No significant differences

were observed between the 2 groups (Fig. 4).

No severe adverse events were reported in this study. Specifically, there were no observed dural punctures in either group, no subdural or intrathecal injections, and no intradiscal injections. No patient in either group sustained any infectious complications, postdural puncture cephalalgia, persistent paresthesias, systemic steroid reactions, skin lesions, or any adverse reaction to contrast media or adjuvant medications. However, in the SP group, 2 patients complained of moderate pain on injection, which was resolved immediately after the injection.



DISCUSSION

Our results showed that the epidural spreading patterns and clinical outcomes of patients undergoing lumbar TFESIs with high-volume injectate were not significantly different between the SP approach and the RD approach, except that the medication exhibited more extensive bilateral distribution in the RD group in 3 mL of injectate.

The effect in TFESI appears to be influenced by the volume of the injected material. Rabinovitch et al (7) reported a positive correlation between fluid injection volume into the epidural space and relief of radicular pain. It was suggested that epidural adhesiolysis washes out inflammatory cytokines from the affected area. Furthermore, the increased volume enables lavage of the epidural space, suppression of ectopic discharge from the injured nerve, and enhancement of blood flow to the ischemic nerve roots (16). In this respect, the injectate volume could have a greater impact on TFESI efficacy than the injectate contents. We therefore decided that an injectate volume of 9 mL would be optimal for epidural adhesiolysis.

The influence of volume on epidural pressure remains controversial. Cardoso et al (17) reported a direct correlation between the volume of anesthetic injected and epidural pressure and Thomas et al (18) also observed higher epidural pressure when larger volumes of local anesthetic were used. In contrast, Paul et al (19) found similar epidural pressures with different injection volumes. Therefore, the decision of when to incorporate high-volume TFESI in patient care should be made at the physician's discretion.

Ensuring good runoff during injection is important to prevent volume-related increase in local pressure. When epidural pressure is increased by injection of fluid, the dura must have been compressed. Dural compression could increase CSF {sp} pressure and CSF absorption. Accordingly, an increase in epidural pressure is transmitted directly to the cerebrospinal fluid, and this in turn will cause a rise in intracranial pressure (20). Moreover, an increase in epidural pressure likely contributes to interference with the blood supply of the spinal cord, causing spinal cord infarction (21,22). A preponderance of patients with this complication are elderly male patients with cardiovascular disease and/or cancer (21,22). Therefore, caution should be exercised in patient selection when performing high-volume TFESI.

Botwin et al (13) analyzed epidurograms after TFESI using the SP approach with a low-volume contrast medium (2 mL). They found that contrast flow extended a mean of 1.13 and 0.6 levels cephalad and caudad from the injection site, respectively. There were no significant differences in contrast flow noted between patients with HNP versus patients with SS. In 3 mL in the SP group, we found that the contrast flow extended a mean of 1.0 and 0.39 levels cephalad and caudad from the injection site, respectively (not shown in Table 2). Moreover, there was no difference in injectate distribution between the 2 groups, regardless of HNP or SS.

Kim et al (23) compared the patterns of contrast spread between the SP and RD approach with lowvolume injectates (1 mL of nonionic contrast medium) in patients with L5 radiculopathy. They reported that the contrast medium diffused around the L5 and S1 nerve roots in 67% of all patients for whom the RD approach was used, whereas the medium diffused around only the L5 root in 73% of all patients for whom the SP approach was used. However, our results showed that the caudad spread was not statistically significantly different between the 2 groups, for either a 0.5 mL or 3 mL injectate volume. Our results showed that 3 mL injectates spread significantly bilaterally in the RD group, which suggests that the RD approach might be more useful when low-volume injectates are used in patients with bilateral symptoms.

Anatomical diversity might explain the slight differences between our results and previous results. The unpredictable spread pattern is likely due to anatomical variation of the epidural space and the complex structure of the epidural space (24). Significant interindividual variation was observed with respect to both area and spread pattern. It is not possible to predict whether the anesthetic will have a cephalad or caudal spread, spread unilaterally, or show a general spread pattern. Burn et al (25) reported that it is impossible to accurately predict the level attained after epidural injection of contrast medium.

The anterior epidural space is isolated from the rest of the epidural space and is nearly filled with veins except for the area caudal to the L4-L5 disk, where a fat-filled anterior epidural space develops (26). Hogan evaluated cryomicrotome sections of the anterior epidural space and found that the anterior space appears to be filled with veins (26) that rarely cross the midplane of the posterior longitudinal ligament (PLL) or its lateral membrane (27,28). The epidural space is filled by a thin layer of areolar connective tissue termed the epidural membrane (29). An anterior midline septum has been identified that divides the anterior compartment (30). Hogan et al (31) also observed a midline tongue of connective tissue extending from the IVD, reaching caudad and to a lesser degree cephalad in the PLL and posterior vertebral body.

Increasing the injectate volume did not result in a linear increase in cervical epidural spread (23). The number of cervical vertebral segments in which 1 mL of epidural medication is distributed is likely to decrease as the injectate volume increases. Regardless of the injected contrast medium volume and the procedure level, epidurography showed more extensive distribution in the cephalad direction compared to the caudad direction (32). These findings are consistent with our results. Moreover, a large-volume injection can clearly show circumferential contrast spread; for instance, epidurograms with 10 mL contrast medium are more clearly opacified than those with 5 mL (33). We found a higher incidence of dorsal spread with 9 mL injectates than with 0.5 or 3 mL injectates, a finding that agrees with previous results that circumferential spread is proportional to volume.

When TFESI is performed, the contrast medium must spread over the proximal region along the anterior lateral part of a specific nerve (34). However, a considerable amount of the drug injected via the SP approach sometimes flows into the distal region along the spinal nerve. This makes it difficult to insert the injection needle in cases of severe SS, when the needle is supposed to be located at the region more anterior to the intratransforaminal epidural nerve root (23). Lew et al (35) have suggested that, because a rostral spread of injectate to bathe the preganglionic portion of the nerve root cannot always be guaranteed, an RD approach at the level of the supra-adjacent IVD could be helpful. Theoretically, by utilizing the RD approach for TFESI, the injectate can be placed closer to the site of neural impingement, thereby providing a more effective washout of inflammatory disc material (35,36). However, a systematic review and meta-analysis of TFESIs with the SP and RD approaches reported that the VAS scores of the 2 techniques were not statistically significantly different (37). Our results also showed similar pain reduction between the 2 groups.

Using the RD approach, the needle tip may unintentionally be placed too far ventrally and enter the IVD. Levi et al (38) performed 257 RD TF injections, and demonstrated a 4.7% rate of intradiscal injection. Needle entry into the IVD may be of concern for several reasons. First, infectious discitis, which is a rare occurrence following provocation discography (39). Second, there may be an associated increased risk of future disc degeneration or herniation induced by needle puncture (40). Therefore, decisions regarding use of the RD approach should take into account discogram.

Although there were no serious complications in our study, 2 patients in the SP group experienced temporary severe pain in the lower back and lower extremities during drug injection. This complication was expected, since the drug was injected into a spinal canal that was likely narrowed due to HNP, SS, or epidural fibrosis (41).

This study had several limitations. First, we enrolled only a small number of patients, and the study was not powered to find small differences in spreading patterns or pain relief between the 2 groups. Second, slightly different methods were used in the 2 groups to determine the number of levels at which the injectate was spread. Third, patients with severe SS or HNP were included, and the injected drugs spread to the distal nerve root in some cases. Fourth, we did not analyze long-term outcomes and focused only on the VAS and RMDQ.

Conclusion

In conclusion, epidural spreading patterns and clinical outcomes, including pain relief and reduced functional disability, were not significantly different between the SP approach and the RD approach in patients undergoing lumbar TFESI with a high-volume injectate. Moreover, in TFESI with low-volume injectates, the RD approach might be more beneficial for patients with bilateral symptoms.

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Author Contributions: Dr. PHS and KWJ had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Dr. PHS designed the study protocol. Dr. PHS, YSH and KWJ managed the literature searches and summaries of previous related work and wrote the first draft of the manuscript. Dr. PHS, KWJ, SHY provided revision for intellectual content and final approval of the manuscript.

Conflict of Interest

All authors have no conflicts of interest to report. None of the authors of the manuscript received any remuneration. Further, the authors have not received any reimbursement or honorarium in any other manner. The authors are not affiliated in any manner. All the authors are members of the Korean Society of Anesthesiologists and practicing interventional pain physicians.

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Role of Sponsor

The financial sponsor of this work had no role in the design and conduct of the study or the collection, management, analysis, and interpretation of the data. The sponsor also did not have a role in the preparation or review of the manuscript or the decision to submit.

Information on author access to data

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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