A Prospective Evaluation of Iodinated Contrast Flow Patterns with Fluoroscopically Guided Lumbar Epidural Steroid Injections: The Lateral Parasagittal Interlaminar Epidural Approach Versus the Transforaminal Epidural Approach

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BACKGROUND: Lumbar midline interlaminar and transforaminal (TF) epidural steroid injections are treatments for low back pain with radiculopathy secondary to degenerative disk disease. Since pain generators are located anteriorly in the epidural space, ventral epidural spread is the logical target for placement of antiinflammatory medications. In this randomized, prospective, observational study, we compared contrast flow patterns in the epidural space using the parasagittal interlaminar (PIL) and transforaminal approaches with continual fluoroscopic guidance.

METHODS: Sixty adult patients with low back pain and unilateral radiculopathy from herniated or degenerated discs were enrolled. Subjects were randomly assigned to one of two groups: TF or PIL (30 in each). All procedures were performed using continual fluoroscopic guidance and 5 mL of contrast. Contrast spread was rated (primary outcome measure) by the interventionalist. Spread was scored 0–2, with 0 = no anterior spread; 1 = anterior spread, same level as needle insertion; and 2 = anterior spread at ≥1 segmental level. The secondary outcome measure was analgesia at 2 wk, 1, 3, and 6 mo.

RESULTS: One hundred percent (29 of 29) patients in the PIL group and 75% (21 of 28) patients in the TF group demonstrated anterior epidural spread. The mean spread grade was 1.93 (95% confidence interval [CI], 1.83–2.0) in the PIL group and 1.46 (95% CI, 1.17–1.46) in the TF group ($P = 0.003$). Mean fluoroscopy time was 28.96 s (95% CI, 23.9–34.1 s) in the PIL group and 46.25 s (95% CI, 36.27–56.23 s) in the TF group ($P = 0.003$). Visual analog scale scores were equivalent between groups.

CONCLUSIONS: The PIL approach is superior to the TF approach for placing contrast into the anterior epidural space with reduction in fluoroscopy times and an improved spread grade. With increasing attention to neurological injury associated with TF, the PIL approach may be more suitable for routine use.

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Midline interlaminar and transforaminal (TF) lumbar epidural steroid injections (LESI) are two accepted treatments in the conservative care of low back pain with radiculopathy secondary to lumbar disk disease. It is thought that the inflammatory response may be localized at the nerve root/intervertebral disk interface, which is in proximity to the anterior epidural space.[1] Previous studies have demonstrated that with the midline interlaminar epidural injections, the injectate spreads into the anterior epidural space only 36% of the time.[1] As a result, practitioners are increasingly performing TF ESI instead of standard midline interlaminar ESI. The TF approach is a proven technique and has shown analgesic effectiveness in multiple studies.[2–6] Although effective, TF injections sometimes lead to complications including spinal cord injury and permanent paralysis.[7] In an effort to provide a suitable and reliable alternative to the TF approach, we studied the parasagittal interlaminar (PIL) epidural approach. With this interlaminar approach, the injection is performed at the lateralmost part of the interlaminar space instead of the usual midline interlaminar approach. No study has compared the two

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techniques (PIL and TF) in terms of the contrast flow patterns and utility for driving medication into the anterior epidural space. In this randomized, single-blind, prospective study, we investigated the spread of contrast media in the anterior epidural space using fluoroscopic guidance. We also studied the analgesic benefit of choosing the PIL or the TF technique.

METHODS

After IRB approval and informed written consent, 60 adult patients with a history of low back pain and unilateral lumbosacral radiculopathy were enrolled. Correlations of history and physical examination findings with diagnostic imaging (i.e., magnetic resonance imaging, computed tomography scan) were noted. Lumbar disk disease included disk herniations, bulging discs, and degenerated discs, where at least 50% of the disk height was preserved respective to contiguous levels. Patients with histories of previous spinal surgery, LESI(s) in the past year, allergy to drugs used, concurrent use of systemic steroid medications, opioid habituation, and pregnancy were excluded. Patients were randomly assigned to one of two groups using a computer-generated randomization table; group TF and group PIL. The intervertebral level and right versus left sides were determined according to the clinical examination and the results of diagnostic imaging studies. All patients were positioned prone, and standard ASA monitors were applied. The corresponding authors who were supervising Pain Management Fellows performed all injections. Fluoroscopic bi-planar imaging was used, with nonionic contrast (total volume = 5.0 mL) in anterior-posterior (AP) and lateral views. Fluoroscopy time was measured consecutively for all scout films, at each needle adjustment according to the protocol, and for the contrast injection phase. Fluoroscopy use was real-time and continuous (i.e., without interruption) during the contrast injection phase, with all personnel, except for the person performing the actual injection, standing more than 6 ft from the radiation source. For the PIL approach, a 20-gauge 3.5 in. Tuohy-type epidural needle was introduced at the level of demonstrated disk pathology by imaging, at the point corresponding to the lateralmost part of the interlaminar opening at its midlevel as indicated by the direct AP projection on fluoroscopy (no oblique or cephalo-caudad tilt used) (Figs. 1a and b). The needle was advanced directly perpendicular to the skin in a posterior to anterior direction, with the use of the loss-of-resistance to air technique in order to identify the epidural space. The parasagittal orientation of the needle was maintained throughout the procedure. Once the loss-of-resistance was obtained, contrast media, 5 mL (Iohexol-180, Amersham Health, Oslo, Norway) was injected using real-time, continuous fluoroscopy for the entire volume of 5 mL of injectate, and images were obtained in the lateral and AP projections (Figs. 2 and 3). The use

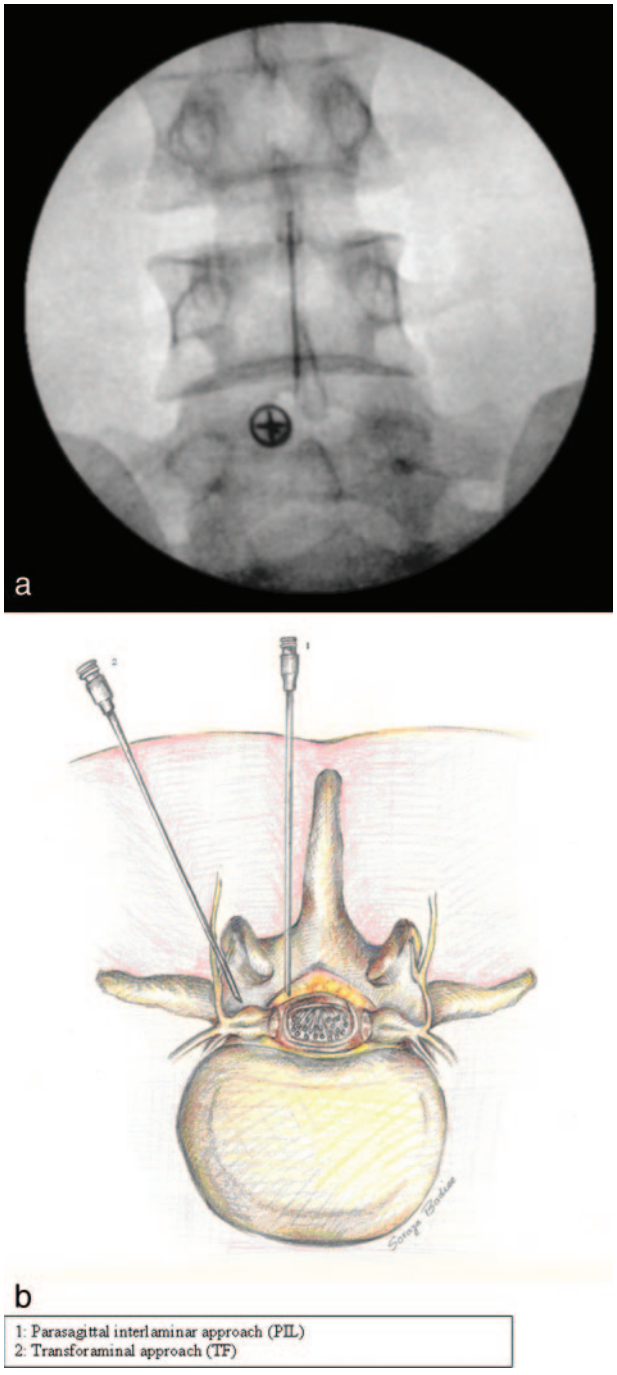

Figure 1. (a) Initial needle entry point for parasagittal interlaminar approach at L4–5 from the left. The midline is defined by the spinous processes where there is a straight needle between the L3 and L4 processes. The tunnel or gun-barrel view is used to follow the trajectory of the needle from posterior to anterior, directly perpendicular to the procedure table. (b) Comparison of the needle entry points for parasagittal interlaminar approach (PIL) versus the transforaminal approach (TF).

of the real-time and continuous imaging was to verify that no contrast attained intravascular, subarachnoid, subdural, or intradiscal spread. Next, the antiinflammatory corticosteroid, methylprednisolone acetate, 80 mg, along with 1 mL of normal saline and 1 mL of lidocaine 1%, was injected into the epidural space (total volume; 4 mL). The saline was added to dilute

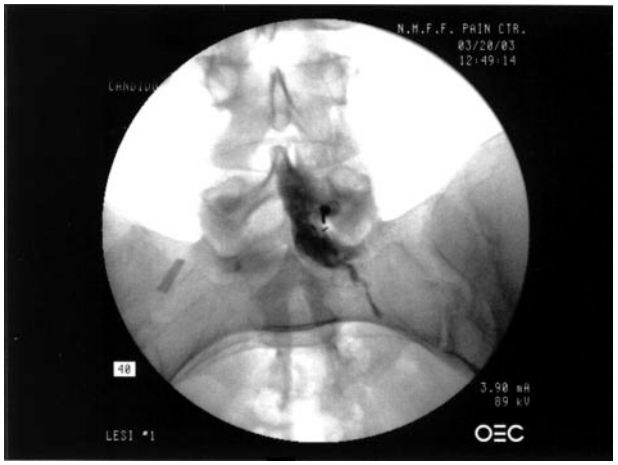

Figure 2. Right parasagittal interlaminar approach; contrast spread L5–S1. Note that the column of dye remains sequestered to the right of the midline as defined by the spinous processes, and also captures more than one nerve root on the right side (see Fig. 1 above).

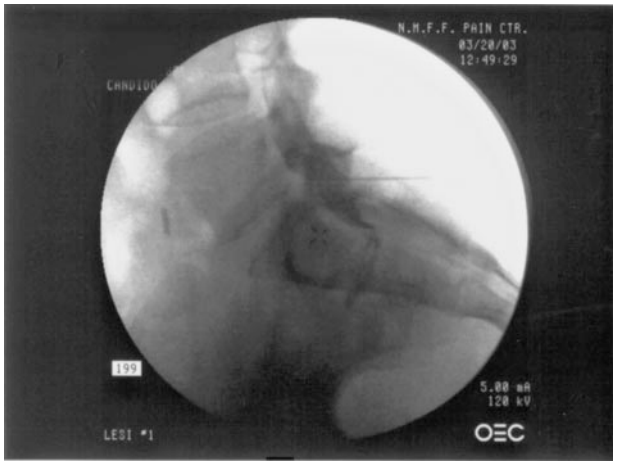

Figure 3. Parasagittal interlaminar approach at L5–S1, lateral projection (same patient as in Fig. 2). Note that the dye spreads both to the ventral epidural space, reaching the posterior longitudinal ligament and posterior vertebral body limit, and that it spreads for multiple segments both ventrally and dorsally. A posterior disk bulge at L5–S1 indents the column of dye, giving it a scalloped appearance.

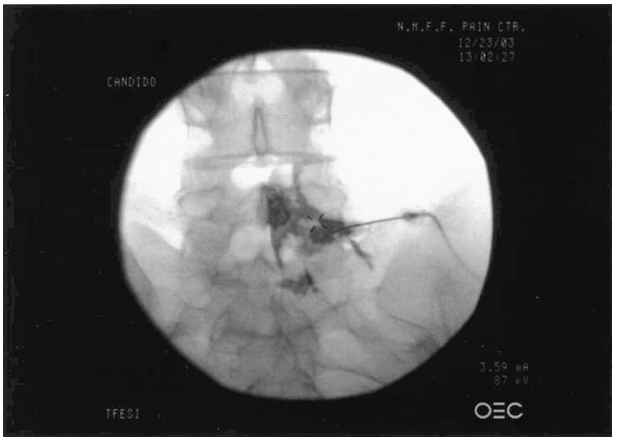

Figure 4. Transforaminal approach at L5–S1, right sided, anterior-posterior projection. Notice the spread of the contrast along the right L5 nerve root, and medially into the epidural space. (Same patient as in Figs. 2 and 3 above; different pain clinic visit).

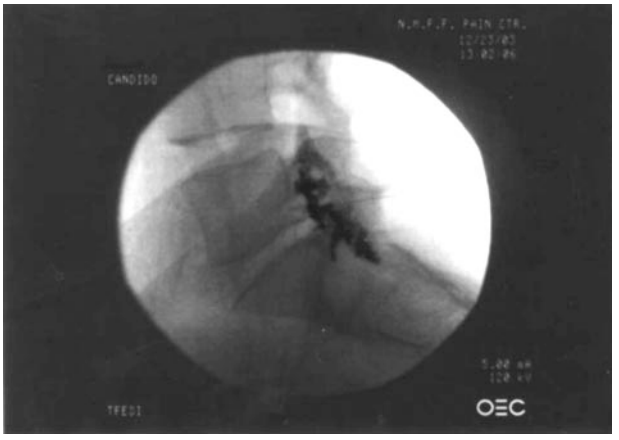

Figure 5. Transforaminal approach at L5–S1 from the right side, lateral projection. Note the spread of contrast ventrally and dorsally in the epidural space extending for more than one segment. (Same patient as in Figs. 2 and 3 above; different pain clinic visit).

polyethylene glycol 4000 (28.6 mg/mL), the vehicle added during manufacture of methylprednisolone that has been implicated to be associated with arachnoiditis. For the TF approach, a 22-gauge 3.5 in. Whitacre pencil point needle with the tip slightly curved was introduced at the appropriately documented level of disk pathology using first an AP and, subsequently, an oblique orientation of the fluoroscopy C-arm.

Once the superior pars interarticularis was identified, the C-arm was oriented obliquely 15 degrees in the caudocephalad direction. The needle was advanced towards the tip of the pars until that structure was contacted, and the needle tip was then advanced in a slightly cephalad direction. The needle was advanced until the needle tip was at the posterior and superior aspect of the intervertebral neural foramen as seen in the lateral projection, and in line with the pedicle on AP view. After incremental injection of the contrast media (Figs. 4 and 5), the same volume and dose of corticosteroid as above for the PIL technique was injected with continual intermittent aspiration. On the lateral projection, the patterns of contrast spread were documented as "anterior" or "posterior" and the degree of spread was quantified using a grading scale from 0 to 2. Zero was equal to "no anterior epidural spread"; 1 was equal to "anterior epidural spread at the same level of needle entry"; 2 was equal to "anterior epidural spread at more than one segmental level from the needle entry point. " Anterior spread was considered present if the dye traveled to the level of the posterior longitudinal ligament or abutted the posterior aspect of the contiguous vertebral body(s) at the level of the needle insertion. An independent blinded radiologist (D.T.), not affiliated with the primary study institution, reviewed the scoring done contemporaneously with the

Table 1. Demographic Data

	TF	PIL
Age (yr)	51.96 (95% CI, 47.05–56.88)	52.31 (95% CI, 46.29–58.32)
Height (cm)	169.80 (95% CI, 165.52–174.09)	169.37 (95% CI, 165.56–173.19)
Weight (kg)	85.21 (95% CI, 78.86–91.57)	81.63 (95% CI, 74.76–88.52)

TF = Transforaminal approach; PIL = Parasagittal Interlaminar approach.

procedures by the interventionalists, viewing only the lateral projection fluoroscopic images from each patient. The percentage of patients demonstrating anterior epidural spread was reported in each group. Also, the total fluoroscopy time and pain relief using verbal analog scale score (VAS) at 2 wk, 1, 3, and 6 mo were evaluated. Sixty patients were included. Group sample sizes of 29 and 29 achieved 81% power to detect a difference of 0.39 between the null hypothesis that both group proportions are 0.36, and the alternative hypothesis that the proportion in group PIL is 0.75 using a two-sided χ^2 test with continuity correction and with a significance level of 0.05.

RESULTS

Two patients in the TF group were excluded from analysis due to the inability of the interventionalist to successfully place the needle tip into the cephalodorsad quadrant of the intervertebral foramina at the level of the pedicle in <60 s of fluoroscopy time (including scout films). One patient in the PIL group was excluded from the analysis because she experienced a nonsustained paresthesia in the low back radiating down the right leg with needle insertion; though no contrast or steroid was injected, the procedure was aborted at the discretion of the treating physician (MR). The data from 57 patients were analyzed. Twenty-eight patients received TF (12 women; 16 men) and 29 patients received PIL (18 women; 11 men). Demographics (age, height, weight) were similar between groups (Table 1). Patient pathologies, interventions, and outcomes are listed in Table 2. The spread of contrast in patients between TF and PIL groups was as follows: all patients (29 of 29) (100%) in the PIL group and 21 of 28 (75%) patients in the TF group demonstrated anterior epidural spread; 28 of 29 (97%) patients in the PIL group had both anterior and posterior spread compared with 18 of 28 (64%) patients in the TF group; and 0 of 29 (0%) in the PIL group had only posterior spread compared with 7 of 28 (25%) patients in the TF group. The mean spread grade was 1.93 (95% CI, 1.83–2.0) in the PIL group and 1.46 (95% CI, 1.17–1.46) in the TF group ($P = 0.003$). Mean fluoroscopy time was 28.96 s (95% CI, 23.9–34.1 s) in the PIL group and 46.25 s (95% CI, 36.27–56.23 s) in the TF group ($P = 0.003$). VAS pain scores at 2 wk were TF 48.85 (95% CI, 37.08–60.61); PIL 40.55 (95% CI, 28.81–52.28) ($P = 0.31$). VAS pain scores at 1 mo were TF 52.77 (95% CI, 40.72–64.83); PIL 52.14 (95% CI, 39.47–64.81) ($P = 0.94$). VAS pain scores at 3 mo were TF 42.93 (95% CI, 29.07–56.78); PIL 46.60 (95% CI, 35.08–58.13) ($P = 0.68$). VAS pain scores at 6 mo were TF 47.07 (95% CI, 36.79–57.36); PIL 41.22 (95% CI, 28.59–53.85) ($P = 0.46$). These data are represented in Figure 6 and show VAS across time. There were no differences from control within either group. The aggregate pain VAS scores were less at all times compared with baseline. The two-way analysis of variance for repeated measures was used to compare these values. There were no observed dural punctures in either group, no subdural or intrathecal injections, and no intrathecal or 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.

DISCUSSION

The use of ESIs and TF injections has been increasing steadily in the United States, even though meta-analyses of their respective efficacies have been less than enthusiastic.[8,9] The rationale for use of steroidal medications neuraxially in low back pain conditions is largely due to the impression that the medication neutralizes the PLA-2 liberated from herniated and degenerated discs.[10,11] Steroids, then, exert an antiinflammatory effect by their demonstrated action by inhibiting PLA-2 and by blocking C-fiber nociception as well.[12]

Notwithstanding the support for an antiinflammatory and antinociceptive effectiveness of steroids, some have suggested that an interlaminar epidural technique of LESI in radiculopathy lacks legitimate rationale and empirical proof of efficacy, since the medication may not reach the target nerve.[13] The target(s) are likely sequestered in the interface of the disk and the exiting root, found in the ventral epidural space. A meta-analysis of all randomized controlled trials related to LESIs showed that they were effective only in the short-term, reducing the need for hospitalization and opioid analgesic requirements.[14] A large prospective randomized controlled trial showed that conventional LESI were effective in the short-term but did not reduce the need for surgery versus placebo control.[15] The presumed failure of long-term success with LESI may be related to the lack of ability to drive the steroid into the ventral or anterior epidural space at the interface of the inflamed nerve root and disk pathology using interlaminar LESI. This lack of anterior epidural placement of medication has been extrapolated to the lumbar situation, from contrast studies of

Table 2. Types of Pathology, Group Assignment, Outcomes in All Study Cases

Patient	Sex	Age (yr)	Group	Baseline VAS (0–10)	Symptom Duration (mo)	Motor Function (LE)	Pathology (HNP, SS, DDD, FS)	Outcome (surgery, further injections, medication mgmt)
1	M	33	TF	8	8	5/5	HNP	NAT
2	F	75	TF	7	>24	5/5	DDD, SS, HNP	NAT
3	M	58	PIL	7	24	5/5	SS	2 PIL; NAT
4	F	57	PIL	10	12	5/5	DDD, SS	3 PIL; SIJ; no change
5	F	67	TF	7	3	5/5	SS, DDD	1 TF; no change
6	M	39	PIL	8	1	4/5	HNP, DDD	Surgery; NAT
7	F	78	PIL	8	7	5/5	DDD, SS	No change
8	F	61	TF	10	>24	5/5	DDD, SS	1 PIL; NAT
9	M	47	TF	6	24	5/5	HNP	1 PIL; NAT
10	F	62	PIL	6	12	5/5	DDD, SS	1 PIL; NAT
11	M	66	TF	5	3	5/5	HNP	NAT
12	F	60	PIL	5	<1	5/5	DDD, SS	1 PIL; NAT
13	F	49	PIL	5	13	5/5	HNP	NAT
14	F	56	TF	8	4	5/5	DDD, FS	1 TF; 1 PIL, NAT
15	M	75	TF	5	12	5/5	SS	NAT
16	F	49	TF	7	2	4/5	HNP	1 PIL; FJB; NAT
17	F	52	PIL	7	>24	5/5	DDD, SS	3 PIL; discography; NAT
18	M	30	PIL	8	10	5/5	HNP	Lost to F-up
19	F	36	PIL	10	2	5/5	HNP	1 TF; discography, PDD
20	F	31	TF	3	>24	5/5	HNP	Discography; no change
21[a]	F	53	PIL	XX	XX	XX	HNP	Paresthesia; dropped out
22	M	41	TF	9	8	5/5	DDD	1 PIL; no change
23	M	30	PIL	8	18	5/5	HNP	NAT
24	M	48	PIL	8	1	5/5	HNP	1 PIL; 1 TF; NAT
25	F	66	PIL	7	4	not stated	SS	2 PIL; FJB; NAT
26	F	51	TF	8	4	5/5	HNP	1 TF; no change
27	M	39	PIL	8	3	4/5	HNP, FS	NAT
28	F	57	TF	5	24	5/5	HNP	NAT
29	F	37	PIL	8	24	4/5	HNP	1 TF; 1 PIL; NAT
30	F	75	PIL	4	2	5/5	HNP, FS	NAT
31	M	57	TF	9	>24	5/5	HNP, SS	1 TF; 3 PIL; NAT
32	M	71	PIL	8	3	5/5	DDD	1 PIL; 1 FJB; NAT
33	F	49	PIL	8	4	5/5	HNP	Lost to f-up
34[a]	M	59	TF	XX	XX	XX	XX	Failure; dropped-out
35	M	69	PIL	4	9	5/5	HNP	5 PIL; no change
36	F	80	PIL	10	5	5/5	DDD	2 PIL; 1 TF; NAT
37	M	80	PIL	6	1	4/5	DDD, SS	1 TF; 1 PIL; NAT
38	M	40	PIL	1	2	5/5	HNP	1 PIL; 1 FJB; 1 SIJ; discography; no change
39	F	58	PIL	8	4	5/5	DDD, SS	3 FJB, 1 PIL; NAT
40	F	54	TF	2	10	5/5	SS	NAT
41	M	50	TF	5	4	4/5	HNP	1 TF; NAT
42	M	49	TF	3	>24	5/5	HNP	No change
43	M	59	TF	5	3	5/5	DDD	Lost to F-up
44	F	59	PIL	9	24	5/5	SS	Lost to F-up
45	M	35	PIL	3	>24	5/5	HNP	No change
46	F	69	TF	8	>24	5/5	DDD, SS	1 TF; 1 PIL; NAT
47	F	39	TF	5	18	5/5	DDD	1 PIL; 2 SIJ; NAT
48	F	30	PIL	3	3	5/5	HNP	NAT
49	M	44	PIL	XX	4	5/5	HNP	NAT
50	F	52	TF	5	>24	4/5	SS	2 PIL; NAT
51	M	25	TF	7	7	5/5	HNP	1 TF, 1 PIL; discography; no change
52	M	50	TF	7	>24	5/5	HNP	1 PIL; no change
53	M	41	TF	8	3	4/5	HNP	4 PIL; NAT
54	M	61	TF	2	8	5/5	HNP	3 PIL; NAT
55	F	49	PIL	3	6	5/5	HNP, SS	1 FJB; NAT
56[a]	M	70	TF	XX	XX	XX	XX	Failure; dropped-out
57	M	53	TF	8	0.5	4/5	HNP	NAT
58	M	52	TF	10	8	4/5	HNP	1 TF, 1 PIL; NAT
59	F	32	PIL	10	>24	5/5	DDD	Lost to follow-up
60	F	36	TF	5	7	4/5	HNP	1 PIL; NAT

HNP = herniated nucleus pulposis; SS = spinal stenosis; DDD = degenerative disc disease; FS = foraminal stenosis; PDD = percutaneous disc decompression; FJB = facet joint blocks; SIJ = sacroiliac joint injections; NAT = no additional treatment needed due to positive response to intervention performed; VAS = visual analog scale; LE = lower extremity.

[a] Dropped out due to failure or paresthesia.

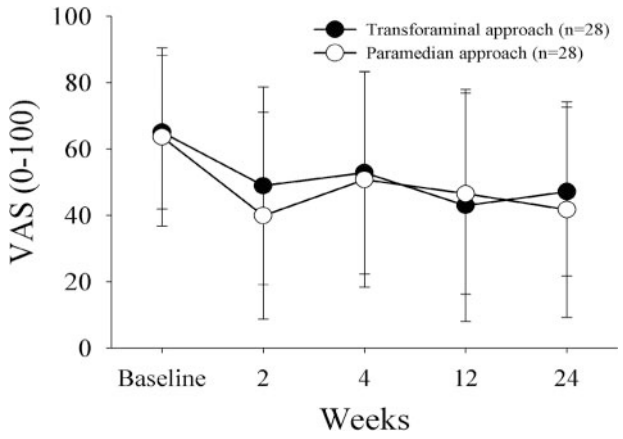

Figure 6. VAS scores across time.

cervical ESI,[16] and has also been evaluated directly using a midline lumbar approach. Botwin et al.[1] conducted a prospective evaluation of epidurography contrast patterns with fluoroscopic-guided lumbar interlaminar injections. In only 36% of cases (9 of 25 patients) was there anterior epidural spread.

The inability to drive the steroid anteriorly in the epidural space has led to a surge in the use of TF blocks.[8] It has also stimulated comparisons of conventional midline interlaminar epidural steroid block with TF block. Lutz and Wisneski[17] reviewed 50 patients with lumbar radiculopathy from herniated nucleus pulposus who responded well to TF ESIs. They postulated that delivery of the medication into the anterior epidural space led to a good clinical outcome. Thomas et al.[18] compared fluoroscopically guided TF and blind interlaminar LESI in 31 patients and noted that the TF approach was superior. Kolsi et al.[19] compared fluoroscopically guided TF and midline interlaminar approaches and were unable to prove whether nerve root injection was superior to an interspinous ligament injection. Kraemer et al.[3] compared perineural conventional epidural and paravertebral local anesthetic injections in the first phase of a two-part study. They then compared perineural steroid and saline. For the epidural perineural technique, the authors used an oblique interlaminar approach, without fluoroscopy. The introducer needle was inserted 1 cm below and 2 cm contralateral, with an angle of 30° to 45° to the midline. The 29-gauge needle then passed the flavum and ended up in the lateral part of the anterior epidural space, which was recognized by bony contact. They studied 182 patients and concluded that the epidural perineural injection was effective in lumbar radicular pain. Manchikanti et al.[20] performed retrospective evaluation of three types of injections: midline interlaminar without fluoroscopy, TF, and caudal injections under fluoroscopy. There were 75 patients in each group. They concluded that the TF and caudal injections were more effective than the midline epidural technique.

A paramedian approach for interlaminar epidural block has been described[21]; however, the use of a fluoroscopically guided PIL approach for the purpose of delivery of medications into the anterior epidural space has not been described. The PIL approach demonstrated a 100% incidence of anterior epidural spread and fared better statistically than did the TF approach. Not only was the procedure highly effective technically, it also took less fluoroscopic time to perform than did the TF approach, leading to less radiation exposure for both the patient and the interventionalist. While the actual fluoroscopy times in the present study appear to be longer than one might encounter in a clinical setting wherein the volume of contrast injectate is on the order of 1 mL, we found the additional time essential in both groups to actually observe the entire flow of the 5 mL of dye in real-time without interruption, including the use of continual, intermittent (q-0.5 mL) aspiration tests.

Complications from TF injections are increasingly being reported. In the editorial accompanying Huntoon and Martin's case report,[7] the very utility of the TF injections was questioned in light of the serious complications, such as paraplegia.[22] Any alternative approach that is potentially safer and offers identical or superior results, vis a vis driving the solution to the ventral epidural space, is most desirable. From a clinical perspective, the results of our study demonstrate an equivalent analgesic response whether the TF or PIL techniques are used. If clinicians could attain identical results with the PIL approach, perhaps the clinical indications for a TF technique in the lumbar spinal area would diminish.

There is no long-term follow-up with our technique past 6 mo, unlike that of Riew et al.[23] for TF nerve root blocks. They showed no difference in outcomes regarding need for surgical intervention between groups treated with bupivacaine TF nerve root injections versus those treated with betamethasone/bupivacaine TF blocks, implying no benefit to using corticosteroids via this approach for improving long-term success. Although this analysis was regarding nerve root or sleeve injections, and not TF epidural injections, the techniques are related anatomically by virtue of the approach and target area of interest. Ackerman and Ahmad noted improved pain scores after TF injections compared with caudal or interlaminar ESI for patients with radicular pain and herniated discs at L5–S1, but used different volumes of contrast and steroid injectates, as well as very large saline volumes in the caudal space (19 mL). It is possible that the significant dilution of the modest dose of triamcinolone (40 mg) used could have resulted in an ineffective concentration of antiinflammatory medication reaching the target(s) to produce analgesia in the caudal ESI patients. They also excluded TF patients if contrast was noted to spread through the foramen at L5–S1, but did not indicate how many patients were thus excluded.[24] In a large retrospective review, Crall et al.[25] showed that needle tip positioning in selective (TF) nerve root injections within or in proximity to the

intervertebral space did not influence immediate outcome, further questioning the requirement to access the nerve root/anterior epidural space using this approach. The same group found a 5.5% "minor" complication rate in 1777 patient visits assessing TF injections. Although there were no reports of permanent neurological sequelae found in that review, we question the need to perform TF injections when the PIL approach would suffice to drive medication ventrally in the epidural space towards the interface of the exiting nerve root (i.e., the target) and the disk pathology (i.e., the etiology of the problem).[26]

We have demonstrated that, in nonoperated lumbar spines, the ability to place contrast media into the ventral epidural space in a timely fashion is more readily accomplished by using the PIL technique than the TF. Each of the supervising physicians has personally performed more than 200 PIL injections and more than 200 TF injections. There were two failures in the TF group due to exceeding the (arbitrary) time limit on radiation exposure, and one PIL patient who experienced a brief and nonsustained paresthesia. One limitation of the present study was the use of different gauge (i.e., 20 vs 22 g) needles for the PIL and the TF approaches. Although this might have affected speed of injection, the use of 5 mL of injectate assured that spread of contrast through the similar gauge needles would not be influenced unduly. Many practitioners inject only 1 mL of solution using the TF technique. Ackerman and Ahmad[24] selected 3 mL, and we selected the 5 mL volume to evaluate and compare where the spread actually goes once the injectate tracks into the epidural space along the nerve root. It is possible that the results attained by using a smaller volume (i.e., 1 or 3 mL) could have been different than those we noted. Additionally, we only controlled the first intervention for each patient; additional treatment decisions were made on a case-to-case basis, limiting our ability to make outcome conclusions in many cases as to the efficacy of one technique over another. Further prospective large-scale multicenter outcome studies are needed to convincingly prove the efficacy and safety of the lateral PIL approach to the anterior epidural space versus TF injections.

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Rasha Snan Jabri, MD suggested the grading scale of 0–2 for quantification of the spread of contrast based upon her experience with Dr. Candido at Northwestern Memorial Hospital in performing a pilot study of the present work in 60 patients (unpublished data) (Figs. 2–5).

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The Efficacy of Lumbar Epidural Steroid Injections in Patients with Lumbar Disc Herniations

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INTRODUCTION: Lumbar epidural steroid injection can be accomplished by one of three methods: caudal (C), interlaminar (IL), or transforaminal (TF). In this study we sought to determine the efficacy of these techniques for the management of radicular pain associated with lumbar disk herniations.

METHODS: Ninety patients aged 18–60 years with L5-S1 disk herniations and radicular pain were randomly assigned to one of these groups to have epidural steroid injection therapy every 2 wk for a maximum of three injections. Pain relief, disability, and activity levels were assessed.

RESULTS: Pain relief was significantly more effective with TF injections. At 24 wk from the initiation of this study, pain relief was as follows: C: complete pain relief: 1/30, partial pain relief: 16/30, and no relief: 13/30; IL: complete pain relief: 3/30, partial pain relief: 15/30, and no relief: 12/30; and TF: complete pain relief: 9/30, partial pain relief: 16/30, and no relief: 5/30.

CONCLUSIONS: The TF route of epidural steroid placement is more effective than the C or IL routes. We attribute this observation to a higher incidence of steroid placement in the ventral epidural space when the TF method is used.

(Anesth Analg 2007;104:1217–22)

The use of lumbar epidural steroid injections (LESI) for the management of radicular pain associated with lumbar disk herniations is controversial (1). There is no consensus on how epidural injection therapy should be done with respect to the volume and mass of steroid injected. In addition, the methods used for epidural injections vary with different physicians, and no standard for the performance of this procedure has been defined. Positive results from epidural steroids vary from 20% to 95% and may depend on route of injection (2). LESI can be accomplished by one of three methods: caudal (C), interlaminar (IL), or transforaminal (TF). Each technique has been reported to be effective for reducing lower extremity radicular pain (3–6). The goal of this study was to test the null hypothesis that these three methods of LESI therapy are equally effective.

METHODS

After patient informed consent and IRB approval, 90 patients aged 18–60 yr were randomly assigned to have LESI therapy every 2 wk for a total of three injections. Each patient in this study had a history and physical examination done prior the initiation of steroid injection therapy. Each patient had radicular pain consistent with the S1 dermatomal distribution. The diagnosis of L5-S1 disk herniations was then documented by magnetic resonance imaging and electromyographic evidence of S1 nerve root involvement.

Subject exclusions included pregnancy, allergies to steroids, steroid use 3 wk or less before beginning this study, bleeding history, infection, use of anticoagulants and allergies to the adjunct medications prescribed while patients were in this study. No patient was included unless they had a pain intensity score >7. Other exclusion criteria were applied after performance of epidural steroid injection (see below) and a complete inclusion/exclusion flow diagram is presented in Figure 1.

LESI was done by one of three methods: (a), C, (b) IL, and (c) TF. Patients were randomly assigned to one of these three treatment groups using computer-generated randomization. IL epidural needle placement was performed with each patient in a prone position. Using an anterior–posterior (AP) view, the L5-S1 interspace was identified by fluoroscopy. The skin was anesthetized with 1% lidocaine and a 22-gauge Touhy needle was directed into the epidural space with fluoroscopic guidance. Each patient received 3 mL of isohexol 300 followed by 4 mL of preservative-free saline with 40 mg (1 mL) of triamincolone after proper needle placement was determined. This volume was used in this study, as it is the volume in our clinical experience that is effective and is between the range of volumes (2–8 mL) used by

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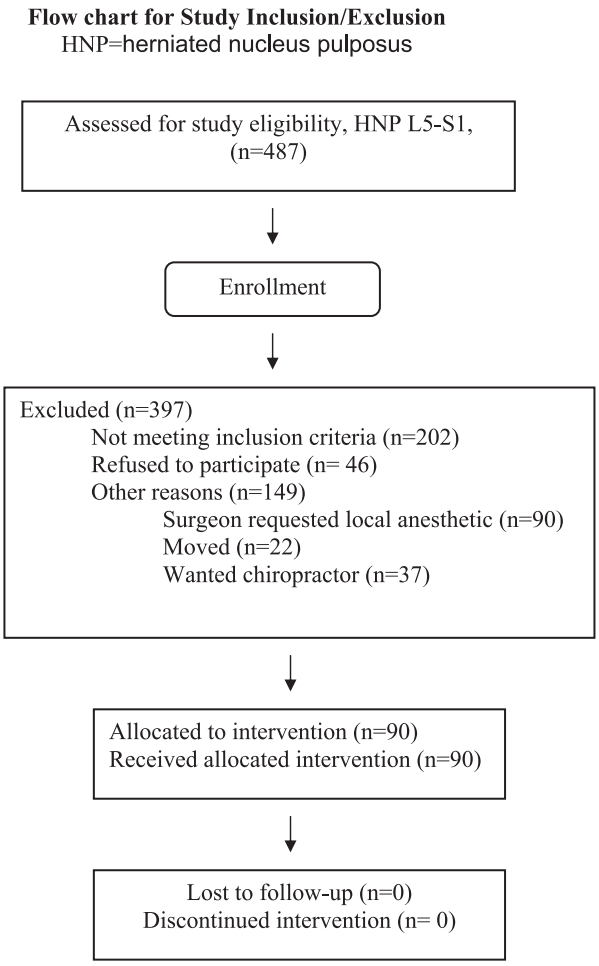


Figure 1. Flow chart for study inclusion/exclusion. HNP = herniated nucleus pulposus.

previous investigators that were reported to be effective as well (4,7). Each needle bevel was directed in a cranial direction. Caudal needle placement was done as follows: each patient was placed in the prone position on the fluoroscopy table. A 22-gauge Touhy needle was guided 1.5 cm into the epidural space from the sacrococcygeal membrane after the skin was anesthetized with 1% lidocaine. Each patient received 3 mL of isohexol 300 injected into the epidural space. After proper needle position was confirmed, 19 mL of preservative-free saline with 40 mg (1 mL) of triamcinolone was administered. This total volume was noted in our clinical practice to be the volume necessary to achieve spread to the L5-S1 interspace and was the volume previously reported by Coomes (8) to be effective. TF epidural needle placement was done with each patient in the prone position. The L5 transverse process on the side of the radicular pain was identified with fluoroscopy. After the skin was anesthetized, a 22-gauge Touhy needle was guided to the transverse process of the fifth lumbar vertebra using fluoroscopic needle guidance. The Touhy needle was used to standardize the needle type used for this study and it is our experience that we could facilitate contrast flow to the anterior epidural space with this needle bevel directed anterior. The needle was withdrawn slightly and advanced medially into the posterior aspect of the L5-S1 foramina. Care was taken to keep the needle tip in the posterior–superior aspect of the foramina because of the increased vascularity in the anterior epidural space and foramina and because of the risk of nerve root injury. The L5-S1 foramen was chosen for the TF group as opposed to the S1 foramen because we noted in our prestudy observations that TF was more effective when the contrast was placed anterior in the epidural space at the level of the disk herniation. Each patient received 3 mL of isohexol 300. Patients were excluded from this study if contrast dispersion with the TF method spread through the foramina at the level of the disk herniation because these subjects would experience postganglion nerve root injection, instead of a TF epidural injection. After correct needle confirmation was obtained, each patient received 40 mg (1 mL) of triamcinolone in 4 mL of preservative-free saline for a total volume of 5 mL (9). For all techniques, IV midazolam 2 mg and 50 μm of fentanyl were used during each procedure. LESI therapy was done without a local anesthetic, as it has been reported that a radicular pain rebound phenomenon occurred when the combination of a steroid and local anesthetic were placed around a nerve root (10).

Patients were observed in a recovery area where hemodynamic variables were monitored and recorded every 5 min for 30 min. Fluoroscopic contrast dispersion was observed at the time of the administration of the steroid saline solution and repeated 30 min postinjection after each patient remained in a supine position in a recovery area. The purpose of the repeat fluoroscopic view was to determine if patient position in the recovery area influenced contrast dispersion. AP and lateral views were analyzed to determine contrast dispersion patterns at the time of the procedure and after patients' recovery time. A physician trained in epidurogram interpretation, who was blinded to the technique used, evaluated each patient's postprocedure epidurogram. Contrast dispersion patterns were identified as ventral (V) (dispersion between the dura and posterior longitudinal ligament); posterior (contrast dispersion between the dura and the ligamentum flavum); and AP (contrast spread both V and posterior) (Fig. 2). Vertical spread was measured to the most cranial vertebral body achieved by the contrast dispersion. Numeric pain intensity scores 0–10 were obtained by an observer blinded to the technique used at the time of each injection and any subsequent injections. Pain relief was placed into one of three categories after each injection: complete pain relief, partial pain relief, and no relief defined by pain scores. The Oswestry Low Back Pain Scale (0–70) and the Beck depression scores (0–63) were recorded by an observer, blinded to the type of LESI that each subject received, at the beginning of this study and 2 wk after each patient's final injection.

Each patient in this study was prescribed tizanidine (6–12 mg/24 hr) as needed for muscle spasms, celecoxib

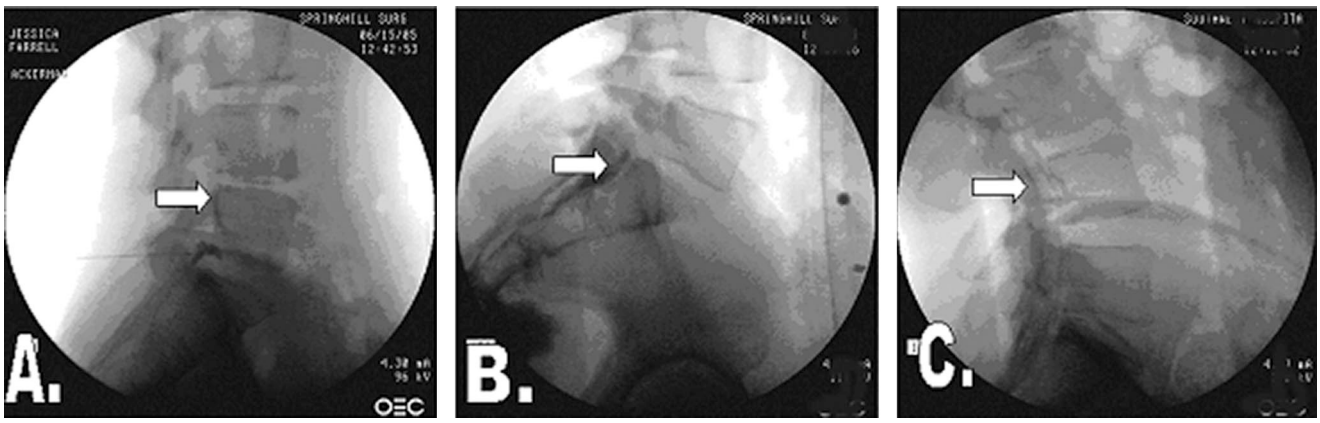


Figure 2. Different lumbar epidural steroid contrast dispersion patterns possible with epidural steroid injections. Epidural contrast dispersion patterns (arrows) with needle placement. A demonstrates spread in the anterior epidural space; B demonstrates spread both anterior and posterior, while C demonstrates a posterior spread.

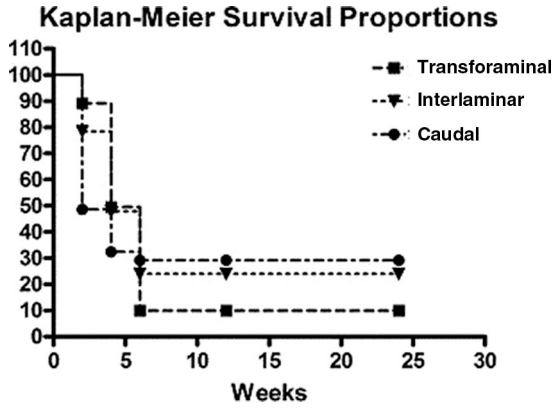


Figure 3. The Log-Rank test (with $\chi^2 = 12.91$, df = 2, P-value = 0.0016) indicates that the survival times (that is, time to pain relief) differ across treatment groups. The median time to achieve pain relief was 2 wk, 4 wk, and 6 wk for caudal, interlaminar, and transforaminal treatment groups, respectively. Symbols placed at observation points.

(100–200 mg) each day as needed for pain and amitriptyline (10–50 mg at night) when they were initially evaluated for this study and while they were participating in it. Each patient was reevaluated 2 wk after initial injection. If a patient had a complete or no pain relief, then no further injection therapy was done. If a patient had partial pain relief (≥4 d to a week from the time of the injection with a visual analog scale score reduction ≥20%) at some time from the injection to the 2-wk reevaluation, a repeat LESI was done. These patients were reevaluated in two more weeks and the same process repeated for a third and final LESI if needed. Subsequently, all patients were evaluated at 12 and 24 wk to determine delayed and long-term efficacy.

Statistical analysis: On the basis of our previous observations of epidural steroid efficacy and our literature search, we determined that a sample size of 30 patients per group was sufficient for this study using a desired power of 0.8 and $\alpha = 0.05$. The primary outcome for power analysis was the pain score.

Statistical analysis was done using Fisher's exact test, ANOVA, χ^2 analysis, the Tukey test, nonparametric distribution analysis and the Student's paired t-test where appropriate with $P \leq 0.05$ required to reject the null hypothesis. Patient data were encoded to protect each patient's identity.

Table 1. Patient Demographics

	Caudal ($n = 30$)	Interlaminar ($n = 30$)	Transforaminal ($n = 30$)
Age (yr)	36.4 ± 4	39.2 ± 6	34 ± 5
Females	11	9	10
Males	19	21	20
Body surface area (m^2)	2.07 ± 0.22	2.11 ± 0.18	2.10 ± 0.21
Duration of symptoms (d)	38 ± 4	33 ± 7	35 ± 5

There were no differences among groups with respect to demographics.

RESULTS

Four-hundred-eighty-seven patients were screened for study inclusion. Figure 1 displays reasons for exclusion. A total of 90 patients were enrolled, completed the study, and were analyzed in groups in which they were allocated (intent-to-treat, Fig. 3). Demographic data are presented in Table 1. One-hundred-eighty-seven LESI were performed: (C = 74), (IL = 67), (TF = 46). Pain relief and associated epidural contrast dispersion patterns are displayed in Table 2. By the 12 and 24 wk evaluation periods, the TF technique had significantly more patients reporting complete or partial pain relief. Pain scores improved within groups but were also significantly lower with the TF approach. (Fig. 4) In terms of mechanism of increased efficacy of TF technique, there was a more frequent incidence ($P \leq 0.05$) of complete pain relief in those patients with the V spread of contrast which occurred more frequently with the TF approach (Tables 3 and 4). Contrast dispersion was not significantly different with respect to cranial vertebral body spread within or across groups. Disability scores were significantly improved within groups as were depression scores but were not affected by injection technique. Function and depression scores improved

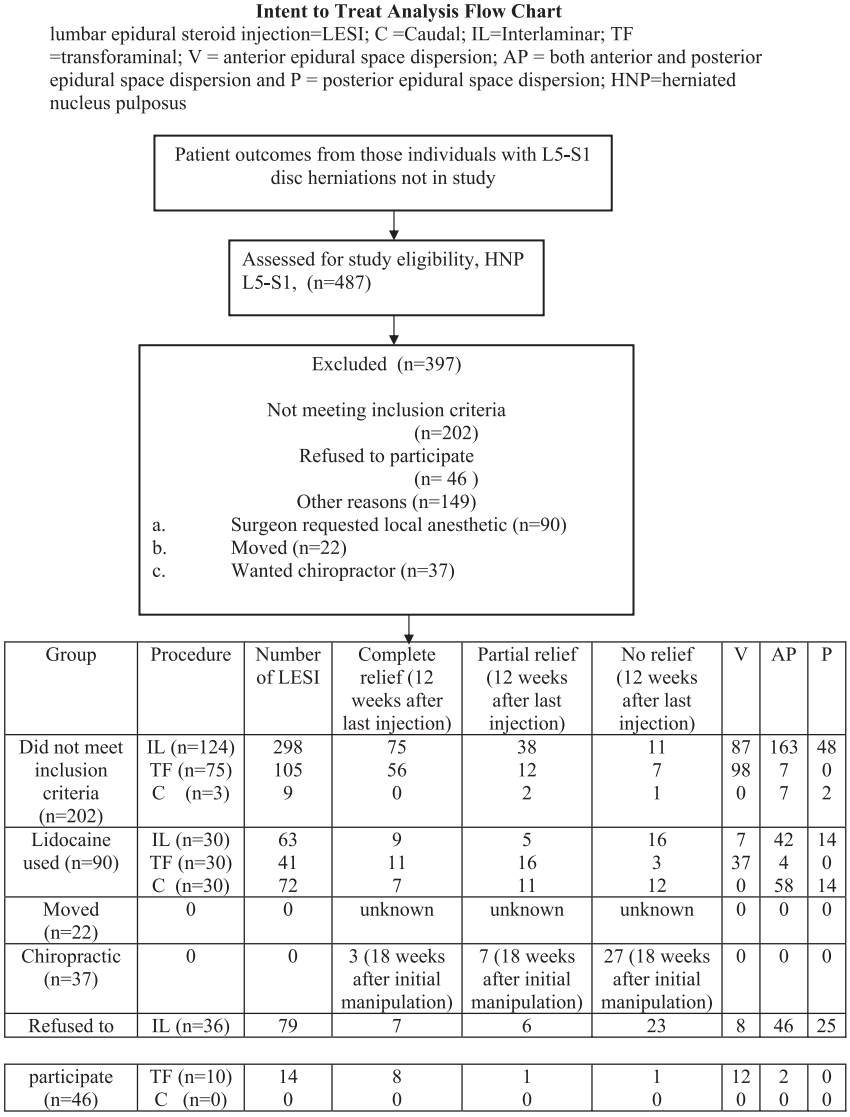
Table 2. Pain Relief and Contrast Dispersion Comparisons Among Groups

Group	*N*	Complete relief	Partial relief	No relief	V	AP	P
C1	30	0.133	0.333	0.534	0.000	0.533	0.467
IL1	30	0.267	0.167	0.566	0.167	0.333	0.500
TF1	30	0.633*	0.267	0.100	0.900*	0.100	0.000
C2	26	0.308	0.346	0.345	0.077	0.654	0.269
IL2	22	0.318	0.273	0.409	0.227	0.455	0.318
TF2	11	0.545*	0.182	0.273	0.727	0.182	0.910
C3	18	0.444	0.444	0.112	0.000	0.778	0.222
IL3	15	0.333	0.400	0.267	0.333	0.467	0.200
TF3	5	0.200	0.600	0.200	0.100	0.000	0.000
C 12	30	0.200	0.367	0.433	0.270	0.635	0.338
IL 12	30	0.267	0.200	0.553*	0.220	0.402	0.373
TF 12	30	0.333	0.500	0.167	0.869	0.109	0.220
C 24	30	0.033	0.533*	0.433	0.270	0.635	0.338
IL 24	30	0.100	0.500	0.400	0.220	0.402	0.373
TF 24	30	0.300	0.533*	0.167	0.869	0.109	0.220
Total injections	187	66	57	64	57	79	51
C	0.396	0.303	0.474*	0.422	0.035	0.595	0.490
IL	0.358	0.303	0.298	0.469	0.263	0.342	0.490
TF	0.246	0.394	0.228	0.109	0.702*	0.063	0.019

One-hundred-eighty-seven epidural steroid injections were done (C (caudal) = 74), IL (interlaminar) = 67, and TF (transforaminal) = 46). Pain relief after injection therapy and contrast dispersion patterns (V = anterior epidural space dispersion, AP = both anterior and posterior epidural space dispersion and P = posterior epidural space dispersion) are given. Statistical analysis done with 3 × 3 contigency Tables.

Indicate with asterisk, which values are statistically different. Include 12 and 24 wk pain relief values. Done.

* Indicates that the proportions of observations in different columns of the contingency table vary from row to row. The two characteristics that define the contingency table are significantly related ($P < 0.001$).



Group	Procedure	Number of LESI	Complete relief (12 weeks after last injection)	Partial relief (12 weeks after last injection)	No relief (12 weeks after last injection)	V	AP	P
Did not meet inclusion criteria (n=202)	IL (n=124)	298	75	38	11	87	163	48
	TF (n=75)	105	56	12	7	98	7	0
	C (n=3)	9	0	2	1	0	7	2
Lidocaine used (n=90)	IL (n=30)	63	9	5	16	7	42	14
	TF (n=30)	41	11	16	3	37	4	0
	C (n=30)	72	7	11	12	0	58	14
Moved (n=22)	0	0	unknown	unknown	unknown	0	0	0
Chiropractic (n=37)	0	0	3 (18 weeks after initial manipulation)	7 (18 weeks after initial manipulation)	27 (18 weeks after initial manipulation)	0	0	0
Refused to participate (n=46)	IL (n=36)	79	7	6	23	8	46	25
	TF (n=10)	14	8	1	1	12	2	0
	C (n=0)	0	0	0	0	0	0	0

Figure 4. Survival analysis for the three study groups. Patients with complete relief had no further injections. The log-rank test (with $\chi^2 = 12.91$, $df = 2$, $P = 0.0016$) indicates that the survival times (that is, time to pain relief) differ across treatment groups. The median time to achieve pain relief was 2, 4, and 6 wk for caudal, interlaminar, and transforaminal treatment groups, respectively. Symbols placed at observation points.

Table 3. Contingency Table Results: Pain Relief and Contrast Spread at 24 wk

	Ventral spread	Nonventral spread	Total
Complete pain relief	10* (11.11)	3 (3.33)	13 (14.44)
Incomplete pain relief	29 (32.22)	48 (53.33)	77 (85.56)
Total	*39 (43.33)*	*51 (56.67)*	*90 (100.00)*

Values inside parentheses indicate percentages.

χ^2 analysis 2 × 2 table. The groups were analyzed comparing complete and incomplete relief with complete ventral and noncomplete ventral contrast dispersion spread. The results are statistically significant ($P \leq 0.05$). Ventral injectate spread positively affects the incidence of pain relief when doing a lumbar epidural steroid injection.

within groups but did not differ among techniques. No patient in this study had an infection, headache, intravascular injection, a reaction to the contrast material, steroid or a subarachnoid injection.

DISCUSSION

In some patients with lumbar disk herniations, conservative pharmacologic and/or physical therapy may not provide adequate pain relief and more aggressive therapies such as LESI may be helpful. An epidural injection can decrease inflammation in the epidural space and can decrease pain in the affected nerve root (11,12). Our study suggests that a TF approach offers benefit for increased analgesic efficacy when compared to the C or IL approach. This may be due to increased V spread of steroid solution with better contact with the herniated disk and extruded contents. Despite this analgesic benefit, no differences were noted between techniques for depression or function, thus functional efficacy may not have differed among groups.

The lack of functional efficacy noted in this study may be related to the fact that we did not have a normal baseline function evaluation that we could compare the abnormal function to prior to the patient's disk herniation. These data would have been helpful in making a statistical comparison.

In addition to potentially differing efficacy, each method of doing a LESI may have complications such as hypotension related to histamine release from the contrast or steroid, systemic toxic reaction, infection, or headache. For the C route, there may be an increased risk of needle tip placement anterior to the sacrum or into the rectum. The chance of puncturing the dura may be less with the C method. The TF method carries a risk of trauma to the nerve root during needle placement. This method also includes the risk of paraplegia if an inadvertent, intraarterial injection of particulate steroid is injected into a radicular artery that reinforces the blood supply of the lower end of the spinal cord (13). Furthermore, disk entry can be a complication of the TF method as well as the IL method (14).

In some instances, the inflammatory process associated with a disk herniation may not be alleviated by nonsteroidal antiinflammatory medications or oral steroids but may be decreased with epidural steroid therapy. Patients in the C and IL groups had increased efficacy with repetitive injections. The reason for this observation is not known but we hypothesize that it could be in part related to repetitive systemic steroid uptake from the epidural veins in the posterior epidural space as well as from blood vessels in the subarachnoid space after steroid passive diffusion across the dura.

This study has limitations: We did not use a double-blind, placebo-controlled group because the patients complained of severe pain, and we did not feel that a placebo injection would be ethical in these circumstances. Inclusion criteria into this study included positive electromyographic studies. The study could have targeted the affected nerve root as opposed to the site of the disk herniation, but our study design called for deposition of steroid in the epidural space as opposed to injecting the S1 nerve root sheath. Another limitation of our study was that the volume of solution we used was not identical. However, because of the large volume of the epidural space in the sacral area, we had to use an increased volume in this anatomic area.

We conclude that, because most lumbar disk herniations are posterior to the vertebrae, inflammation occurs primarily in the V epidural space at the site of the disk herniation (15). Deposition of steroid in the anterior epidural space directly at the site of inflammation may be one reason why patients with injectate spread in the V epidural space had better pain relief

Table 4. Disability, NPIS, and Depression Scores

LESI	*n*	Oswestry score at the initial LESI (0–70)	Oswestry score 2 wk after the last LESI (0–70)	BDI at the initial LESI (0–63)	BDI 2 wk after the last LESI (0–63)	NPIS at the initial LESI (0–10)	NPIS 2 wk after the last LESI (0–10)
C	30	37 ± 9	14 ± 6*	21 ± 11	13 ± 9*	8.9 ± 0.7	6.1 ± 0.8*
IL	30	33 ± 4	13 ± 4*	19 ± 4	11 ± 6*	8.8 ± 0.8	5.7 ± 3.3*
TF	30	30 ± 6	14 ± 9*	22 ± 8	12 ± 4*	8.6 ± 0.9	2.4 ± 2.1*†

Oswestry Low Back Pain Scale and the Beck Depression Inventory (BDI) score at the time of the initial lumbar epidural steroid injection (LESI) and at 24 wk. The numeric pain intensity score (NPIS) was analyzed in a similar fashion. Furthermore, the NPIS was recorded prior to any subsequent LESI and patients with NPIS = 0 were not followed for a repeat LESI (C = caudal, IL = translaminar, TF = transforaminal).

* $P < 0.01$ within group (means ± SD).

† $P < 0.05$ with respect to groups C and IL.

than those with posterior epidural contrast dispersion patterns.

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In Response:

In this controlled, randomized, prospective study (1), we analyzed the safety and efficacy of midazolam and propofol, taken alone or in combination, for prolonged sedation of trauma patients. Patients in all groups received morphine as an analgesic, at similar dosage (Table 2 of Reference 1); none of the patients suffered renal failure (inclusion criteria: serum creatinine <2 mg/dL).

In our study, we differentiated between two patient groups: those without severe head injury (in which we evaluated wake-up times after sedation and analgesia withdrawal), and those with severe head injury (in which we evaluated Glasgow Coma Score evolution). Because this study was a prospective-randomized trial, in which morphine doses were similar for all groups, we believe that the differences found between the groups resulted from the different sedative protocol administered.

We think that the Glasgow Coma Score evolution observed in our patients, as well as the subsequent length of stay, is caused by the underlying disease, instead of the administration of morphine, which, when compared with others like fentanyl (2), has a reasonable elimination half-life in the absence of renal failure. In our patients, we did not observe the presence of renal dysfunction (inclusion criteria); this condition as Takahashi et al. have outlined, could have prolonged the conscience level recovery of our patients.

Finally, our experience is different from that referred to by Takahashi et al. We did not find a significant lengthening in our patients' waking times under prolonged continuous administration of morphine (including in the presence of renal dysfunction). We believe that the combination of efficacy and cost, as well as the absence of significant adverse effects, renders morphine chloride an effective drug for prolonged analgesia in the severely traumatized patient.

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Fluoroscopy Is Medically Necessary for the Performance of Epidural Steroids

To the Editor:

We read with great interest the article by Fredman et al. (1) titled "Epidural steroids for treating 'failed back surgery syndrome:' is fluoroscopy really necessary?" This well designed and well conducted study described the implications appropriately, but it did not draw the conclusion that fluoroscopy is medically necessary to perform epidural steroids in the treatment of "failed back surgery syndrome." As they correctly point out, despite accurate placement, the depot-steroid solution will spread to reach the level of pathology in only 26% of cases. If one considers this as the average delivery, and with an average success rate of 60% for epidural steroid injection(s), this would translate into a 16% success rate. However, if one believes that the cardinal site of pathology is considered to be in the ventral epidural space, the results look even more disappointing when using a blind epidural injection (2,3).

Several approaches available to access the lumbosacral epidural space are caudal, interlaminar (lumbar), and transforaminal (nerve root or selective epidural injections) (2,3). As stated by the authors (1), the interlaminar approach for lumbar epidural has been perceived as advantageous, because the needle is directed more closely to the assumed site of pathology, facilitating the injectate's delivery directly to its target. However, when using a blind interlaminar technique, one may erroneously miss the targeted interspace by one or two levels. The preferential cranial flow of solutions in the epidural space necessitates the needle's position one level below the site of suspected pathology, and the epidural needle placement may significantly deviate toward the nondependent side, thus negating the presumed benefits (4–9). Other potential difficulties encountered with lumbar epidural injections include congenital abnormalities, postsurgical spine as described, and target specific placement of injectate at L5/S1 (10). Hence, transforaminal epidural injections have been considered the most advantageous in reaching the cardinal site of the pathology under direct fluoroscopic visualization with an extremely low dose of steroids. Based on this report (1) and others in the literature (4–9,11), without the use of fluoroscopy and epidurography, additional risks can be foreseen with epidural steroid injections because of the increased potential for dural puncture, subarachnoid injection, and intravascular injections with associated complications. Performing a procedure that only has the effectiveness of 16% based on the present data (1) is definitely not a cost-effective procedure. However, whether fluoroscopy and epidurography add any risks is an important question. Radiation exposure is minimal in experienced hands, has a low risk of allergic reaction, and is minimized and almost entirely eliminated by using low volume, nonionic contrast media. At least in the United States, the additional cost of the procedure with fluoroscopy should be immaterial in an ambulatory surgery setting at the present time, because surgery centers are paid for the facility based on global charges regardless of whether fluoroscopy was utilized. With new regulations scheduled to be implemented in hospital outpatient departments, the same global structure will be used with no extra cost for using fluoroscopy and epidurography. In fact, there will be tremendous cost savings by insuring that the epidural space has in fact been reached, thereby reducing failures by as much as 50% to 60% by avoiding misinjection.

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In Response:

Although it seems that Manchikanti et al. support the use of fluoroscopy, we disagree with the conclusion that fluoroscopy is medically necessary in all cases of "failed back surgery syndrome" (FBSS). Furthermore, in our opinion, they do not provide convincing evidence to support their preference.

Manchikanti et al. criticize the fact that we have not "drawn the conclusion that fluoroscopy is medically necessary to perform epidural steroids in the treatment of [FBSS]." However, our data do not support such an emphatic conclusion. Rather, as stated in our original manuscript, in patients who have undergone surgical "procedures associated with extensive tissue trauma or in which the

posterior spinous processes are removed, fluoroscopy may ensure more accurate epidural space identification." Thus, we suggest that "the surgical records may be vital when analyzing the cost-benefit of fluoroscopic guidance."

Manchikanti et al. conclude that, in the absence of fluoroscopy, epidural steroid administration would be associated with a "16% success rate." However, our study demonstrates that simple mathematical proportions are not reliable when predicting the success rate of epidural steroid placement in FBSS. Although blind needle placement was accurate in 47% of patients, spread of contrast medium within the epidural space reached the level of pathology in only 26% of patients. Because, in FBSS, the limited spread of contrast medium (or depot-steroids) is likely caused by surgically induced adhesions, in our opinion, it is doubtful that fluoroscopy would significantly improve target tissue penetration.

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Conclusions Regarding Propofol/Lidocaine Admixture May Be Misleading

To the Editor:

Wachowski et al. (1) stated "We conclude that clinically relevant concentrations of lidocaine, when mixed with the propofol emulsion, do not prevent the growth of *S. aureus, E. coli,* and *C. albicans.*" This broad generalization may be misleading. As noted in the article, growth inhibition of bacteria and fungi by lidocaine is altered by pH, concentration, and temperature. Wachowski et al. (1) failed to demonstrate growth inhibition of *S. aureus* in mixtures of propofol containing 5 mg/mL lidocaine hydrochloride at 20°C (68°F). This temperature was used to mimic conditions within an operating room. In a similar study, we determined that an admixture of propofol with a lidocaine hydrochloride concentration of 5 mg/mL resulted in significant growth inhibition of *S. aureus* at 37°C (2). Although many operating room sites are kept at reduced temperatures, other operating room sites such as those for pediatric surgery or trauma surgery are maintained at temperatures significantly higher than normal room temperatures. The admixture of 5 mg/mL to 10 mg/mL lidocaine hydrochloride with propofol may increase safety by inhibiting the growth of some microorganisms at temperatures >20°C. The mean inhibitory concentration of lidocaine hydrochloride ranges between 2.5 mg/mL to 40 mg/mL (3–5). This range in concentrations may reflect variations in temperature, pH, and the variability of resistance by different organisms. In addition, the pKa (pH at which the concentration of ionized and unionized forms are equal) of lidocaine hydrochloride is 7.9, and only the nonionized fraction appears to be active in microbial growth inhibition. Wachowski et al. (1) determined the mean pH of the solutions in the study and found that the lidocaine/propofol admixtures were as acidic as 0.5% lidocaine alone. In our study, we used 4% lidocaine to formulate the propofol lidocaine admixtures to minimize the volume of the acidic lidocaine in the final mixture. Because we (2) did not determine the pH of our solutions and Wachowski et al. (1) did not describe the formulations of their mixtures, no direct comparison of the effect of pH on the ability of lidocaine hydrochloride to inhibit microbial growth can be ascertained between the studies. A detailed analysis of the effects of temperature, concentration, and pH on inhibition of microbial growth with lidocaine hydrochloride and propofol admixtures would help determine the differing findings of these two studies.

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In Response:

We thank Dr. Driver for his observations and comments. Dr. Driver correctly identifies two of the factors that are potentially confounding variables in microbial studies of this nature, pH and temperature.

We highlighted the relationship between temperature and the growth of *S. aureus* in the paper by Crowther et al. (1). In that study, we were not able to document a significant growth of *S. aureus* in propofol at 20°C in contrast to the report of Sosis and Braverman (2), which clearly documented significant growth in propofol after 6 h at 27°C. We had used the same *S. aureus* strain (ATCC 25923) and similar methodology. Temperature was the only variable that accounted for this discrepancy.

Taki et al. (3) addressed the issues of temperature and lidocaine concentration on the growth of *S. aureus*. They demonstrated that at 37°C, a lidocaine concentration of 0.5% (5 mg/mL) was the highest concentration of lidocaine that permitted *S. aureus* to grow after 6 h. Concentrations of lidocaine greater than this resulted in the decline of bacterial viability. They also observed that, at 10°C, a lidocaine concentration of 1.0% resulted in no decline of the viability of *S. aureus*. Furthermore, at 40°C, lidocaine 0.25% produced a conspicuous decline of bacterial viability. This work confirms that the inhibitory actions of lidocaine toward *S. aureus* are concentration and temperature dependent.

The report of Berry et al. (4) speculated that pH is a mechanism of the bactericidal activity of thiopentone. The high alkalinity of thiopentone accounted for its bactericidal activity, a property that Crowther et al. (1) demonstrated could be transferred to an admixture of thiopentone and propofol.

Although our generalization in the paper by Wachowski et al. (5) was broad, it remains accurate. It is also supported by the recent work by Vidovich et al. (6), who concluded that the addition of lidocaine to propofol in concentrations clinically effective in reducing pain on injection had no effect on microbial growth. As Dr. Driver correctly proposes, studies with any admixture involving propofol must be carefully conceived and executed. Not only must pH and temperature be carefully documented, but the strain of bacteria used must be clearly identified, because not all strains of *S. aureus* are inhibited by even 2% lidocaine (7). Likewise, methodological differences can confound comparisons between studies. In Dr. Driver's abstract (8), baseline colony counts in the various mixtures are not presented. Therefore, conclusions regarding relative growth between the mixtures should be interpreted with caution. We chose a methodology similar to Sosis and Braverman (2) to compare our results. As it turned out, this allowed us to consider the role of pH and temperature on microbial growth in our papers by Crowther et al. (1) and Wachowski et al. (5).

We concur with Dr. Driver that a detailed analysis of the effects of temperature, concentration, and pH on the inhibition of microbial growth with any admixture involving the propofol emulsion is necessary. However, we suggest that any conclusion that implies that an admixture of lidocaine with propofol may increase patient safety by inhibiting the growth of some microorganisms at temperatures >20°C is intrinsically flawed. Inhibition of microbial growth is not the same as microbial destruction. Any inhibitory effects of the admixture may rapidly dissipate after introduction into the patient. Once introduced into the circulating blood volume, the concentration of lidocaine would become barely detectable. As has been documented with *E. coli,* those bacteria not irreversibly damaged would again be able to propagate and pose a life-threatening risk to the patient (9). Consequently, any alteration of the propofol emulsion that does not confer bactericidal properties to the resulting