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Randomized Trial

Interlaminar Versus Transforaminal Epidural Steroids for the Treatment of Subacute Lumbar Radicular Pain: A Randomized, Blinded, Prospective Outcome Study

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Background: There is uncertainty in the literature over the relative effectiveness of lumbar epidural interlaminar (IL) steroid injection versus transforaminal (TF) steroid injection for lumbar radiculopathy. Most studies to date have been retrospective, or technically focused.

Objective: To complete a randomized, blinded, prospective outcome study of the short-term benefit for IL versus TF epidural steroids for the treatment of subacute lumbar radicular pain.

Study design: Prospective, randomized, blinded, subacute efficacy trial.

Setting: Tertiary care pain management center, major metropolitan city, United States

Methods: After institutional review board approval, 42 age-matched patients with similar lower back pain and unilateral radicular symptoms were enrolled and randomized in a patient and evaluating physician blinded trial to IL or TF epidural steroids from 2007 through 2009. Prior to intervention and 10-16 days after injection, each participant was evaluated by questionnaire and physical exam by an independent physician. All injections were performed by the same physician. Thirty-eight participants completed the study, 18 in the IL group and 20 in the TF group. Four participants required a repeat injection, and 2 participants crossed over to the alternative injection type (IL to TF).

Results: Overall, physical exam, diagnostic testing, disability, activity, depression measures, and opioid pill use were similar between the 2 groups, both pre-injection baseline and post-injection improvement. In primary outcomes, the post-injection follow-up Numeric Rating Scale (NRS) was more greatly reduced in the TF group. The NRS decreased from 7.0 ± 1.9 to 3.9 ± 3.1 (mean values +/- standard deviation) in the IL group and 6.4 ± 2.1 to 1.7 ± 1.4 in the TF group. The Oswestry Disability Index was reduced from 37.5 ± 12.6 to 19.0 ± 16.7 in the IL group and 38.3 ± 6.4 to 21.6 ± 16.8 in the TF group. In secondary outcomes, the depression scale was reduced from 4.39 ± 3.22 to 2.28 ± 3.20 in the IL group and 4.10 ± 1.94 to 1.65 ± 1.63 in the TF group. Walking tolerance was increased from 8.1 ± 4.6 blocks to 10.6 ± 4.4 in the IL group and 8.9 ± 5.3 blocks to 11.8 ± 4.2 in the TF group.

Limitations: The study did not examine long-term outcomes. A single experienced interventionalist performed all injections.

Conclusion: Results suggest that patients may experience greater subjective relief, at least initially, from TF epidural steroid injections over IL. However, more objective, and likely subacute, therapeutic effects are similar.

Key words: epidural, steroids, interlaminar, transforaminal, lumbar, lumbosacral, radicular, low back pain

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A multimodal, multidisciplinary approach, focusing on short-term analgesics, physical therapy, and patient education, is the mainstay for management of low back pain (1). Since epidural analgesia's introduction (2,3), and later the use of epidural steroids (4-10), it's long been accepted that mechanical causes of back pain, accompanied by signs of nerve root irritation, may respond to epidural steroid injections (ESIs)(5-17). Steroids presumably exert their effects by limiting inflammatory response from injuries, inhibiting leukocyte aggregation, preventing degranulation of inflammatory mediators, stabilizing lysosomal and other membranes, and reducing the synthesis and release of proinflammatory factors (11). Over the past two decades, lumbosacral steroid injections have been increasingly utilized for the diagnosis and treatment of low back pain (16-19). While the long-term benefit of epidural steroid is argued (5-10,12-17), short-term pain benefit from weeks to months for subacute pain is accepted (5-10,12-17). The landmark double-blinded clinical study of interlaminar (IL) epidural steroids versus isotonic saline into the epidural space only demonstrated modest benefit for epidural steroids in the first 3 to 6 weeks and no difference in those pursuing surgery (15). Multiple blind studies have found similar results, with ESIs being favored for short-term symptomatic treatment of low back pain with radiculopathy (20,21).

Some studies have suggested superiority for transforaminal (TF) ESIs for low back pain with radiculopathy in both short-term and long-term outcomes (13-17). Schaulfele et al (22) presented evidence that TF ESIs are superior to IL injections for acute pain treatment (2-3 weeks) (14). Ackerman et al (23) in 2007 also demonstrated TF superiority to IL epidural steroid injections for lumbar radicular pain with respect to the numerical pain score in a randomized, prospective fluoroscopic-guided study.

Previous reviews show that the long-term benefit for TF steroid injections appears likely (6,14,24,25), and less likely for IL (13,15,16), while the short-term benefit (weeks to months) is established for both techniques (6,12-15,24,26-28). More recent and fluoroscopically directed studies show an equivalent benefit for lumbar interlaminar and transforaminal injections (29-31,33,42). Fluoroscopically directed caudal epidural injections appear to have similar efficacy as well (32,37-41), caudal technique cross comparison with TF ESI is less commonly expored and discussed in the literature. Thus, we present a randomized, blinded, prospective outcome study of the short-term benefit of IL versus TF epidural steroid injections for the treatment of subacute lumbar radicular pain.

Methods

Participants

After Institutional Review Board approval was obtained, 42 patients with low back and radicular pain were enrolled into this prospective, randomized, blinded, crossover cohort study. They were initially referred to the outpatient pain clinic by a preselected group of specialists including neurologists, neurosurgeons, orthopedic surgeons, rheumatologists, and rehabilitation physicians who were familiar with the selection criteria. The enrollment took place from October 2007 through February 2009 in a major metropolitan tertiary care pain center. All participants had failed conservative therapy including elapsed time, a trial of multiple pharmacologic analgesic agents, physical therapy, and other nonspinal injections, but had not undergone ESIs (in the previous 6 months) or surgical interventions. Each participant underwent a thorough standard evaluation by a single pain physician, which included an evaluation of their clinical history, physical examination, x-rays, computed tomography (CT) or magnetic resonance imaging (MRI), and electromyogram (EMG) of the lower extremities.

Inclusion and exclusion criteria are described in Table 1. Participants were randomly assigned to one of 2 groups using a computer-generated randomization table: Group TF or Group IL.

Prior to the first ESI, the evaluating physician, separate from the physician performing the spinal injection, performed a baseline assessment and recorded the clinical history, physical examination, sitting straight leg raise results, the Oswestry Disability Index (ODI), NRS of daily pain, NRS for depression, NRS for tolerance to physical therapy, number of blocks able to walk consecutively before stopping due to pain, average number of opioid pills consumed in one day, diagnosis/etiology and laterality, and spinal levels that were recommended to be injected. Allocation to injection type was randomly computer determined before this step, the assessing physician was blind to this information. During the course of the study all participants continued to receive other treatments such as physical therapy and their baseline pharmacologic analgesic agents, with the exception of new analgesic agents, additional peripheral injections, central injections, or surgery.

Table 1. *Inclusion and exclusion criteria*

Inclusion Criteria	Exclusion Criteria
Chief complaint of low back pain radiating to one lower extremity	Previous lumbar spine surgeries or epidural steroid injections in the previous 6 months
Failed analgesic and nonpharmacologic therapy trial of at least one month	Multilevel degenerative spine disease, unstable spine, spondylolisthesis (> grade 1), spondylolysis
Duration of current back and leg pain for greater than one month and less than a year	Cauda equina syndrome, arachnoiditis, progressive neurologic deficit
Symptoms due to acute, or sub-acute, disc disease	Central spinal canal stenosis (congenital or acquired) from other origins, vertebral compression fracture(s)
Correlation between the clinically determined level(s) of radiculopathy and the findings on CT or MRI.	Active cancer diagnosis, history of substance abuse, current psychiatric co-morbidity, pregnancy
Inability to tolerate physical therapy or no benefited from ongoing physical therapy	Myelographic contrast allergy, steroid allergy, local anesthetic allergy
Ability to read and write in English	Ongoing medicolegal or workman's compensation proceedings

Sample Size

The sample size was determined based on a review of past literature and power analysis. Previous comparative epidural steroid studies have employed sample sizes of 20-30 participants per treatment group (22-24,29,30). Studies that included radicular symptoms due to spinal stenosis or chronic degenerative disease (as opposed to acute or subacute disc herniation) did not typically find statistically significant differences between treatment groups (29,30). Previous studies focusing on acute and subacute disc herniation pathology had seen statistically significant differences ($P < 0.05$) in treatment modalities with 20 to 30 participants per group (22-24). A power analysis based upon these previous studies suggested that statistically significant differences between groups, using t test analysis, would be seen with 20 participants for each injection type, assuming an approximate 20% difference (or greater) and standard deviations similar to previous studies cited. Upon enrollment of 42 participants, significant power was achieved with respect to primary outcomes and enrollment was stopped.

Interventional Techniques

A single pain physician with over 10 years of experience with both techniques performed all ESIs in a uniform fashion, thereby eliminating an inter-physician technique variability. The interventionalist was blind to participant data that was not needed to safely perform the required injection.

Interlaminar Epidural Steroid Injection Technique

The participant was positioned prone with a pillow under the abdomen. Anteroposterior (AP) imaging was obtained to identify the desired interlaminar space. The superior border of the ipsilateral lower lamina was marked and the skin and tissue overlying the target point was infiltrated with 1% lidocaine using a 25-gauge, 1.5-inch needle. An 18-gauge Tuohy needle was advanced toward the epidural space under AP and lateral fluoroscopic guidance. Loss-of-resistance-to-air was the primary sign of entry into the epidural space. Once the epidural space was entered, a lateral fluoroscopic view was obtained to ensure that the needle tip rested in the posterior epidural space. Then iohexol 180 contrast medium was injected in 1 mL increments up to a maximum of 5 mL until ipsilateral epidural placement (to the side of the pain complaint) was confirmed. If the physician was unsuccessful at gaining epidural access at the predetermined IL level, then an adjacent IL level was attempted. Once epidural placement was confirmed, 2 mL of 40 mg/mL triamcinolone diacetate and 2 mL of 0.25% bupivacaine, for a total of volume of 4 mL, was injected.

Transforaminal Epidural Steroid Injection Technique

The participant was positioned prone with a pillow under the abdomen. AP imaging was obtained to identify the desired spinal level followed by an ipsilateral oblique angle. The 6 o'clock position of the pedicle was marked and infiltrated with 1% lidocaine using a 25-gauge, 1.5-inch needle at 2 levels. Two 22-gauge 3.5-inch spinal needles were directed under intermittent fluoroscopic guidance into the neural foramens such that the tip rested within the triangle composed of the nerve root medially, the bony pedicle superi-

orly, and the lateral border of the foramen laterally. The needle positions were confirmed by observing the flow of 1 mL of iohexol 180 contrast medium injected at each level. One milliliter of 40 mg/mL triamcinolone diacetate mixed with 1 mL of 0.25% bupivacaine for a total of 2 mL was injected at each level with a total injectate volume of 4 mL.

Outcome Measurements

Primary outcome measurements included the NRS for daily pain and the ODI score (32,33,37-46). Secondary outcome measurements included subjective measurements of depression and the ability to tolerate physical therapy as well as the participant's own measure of the number of consecutive blocks walked before stopping due to excessive pain, and average number of opioid pills consumed each day.

Ten to 16 days following the initial ESI, the evaluating physician who was blinded to the type of ESI performed, reassessed each participant with the "ESI Follow-Up Evaluation Form" with additional questions including the patient's response to lumbar ESI (either > 75% relief; < 75% relief, but satisfactory subjective improvement; or < 75% relief). Following the initial ESI, if a participant had > 75% relief or < 75% pain relief that they were satisfied with, they were indicated for routine follow-up in one month or follow-up with their referring physician for further care. If following the initial ESI, they had < 75% relief and did not feel subjective satisfactory improvement, then they were eligible for a second ESI of the same type as the original injection.

The second ESI of the same type was performed 2 to 4 weeks after the initial ESI. Ten to 16 days after the second ESI each participant was once again evaluated in the same fashion with same exit criteria. Following the second ESI, if participants had < 75% relief that was unsatisfactory, then they were eligible for crossover to the alternative ESI type. At crossover, participants who had previously had 2 TF ESIs were now eligible for an IL ESI and those who had previously received 2 IL ESIs were now eligible for a TF ESI. The third ESI was performed 1 to 2 weeks after the follow-up visit. Ten to 16 days after the third ESI, each participant was evaluated in the same fashion as performed in the prior post-injection visits.

Statistics

A t test comparison was applied to all baseline pre-injection and post-injection values at 10 to 16 day follow-up, comparing the IL and TF groups, using a 2-tailed t test. Within the IL and TF groups, pre-injection values were compared to post-injection values at 10 to 16 day follow-up, also using t test comparison. Results were considered statistically significant if the P value was less than 0.05.

Results

Participant flow is illustrated in Fig. 1.

There were no changes to trial methods or outcomes after the study's commencement. A total of 42 patients were enrolled in the study, among which 21 were randomized to receive a TF injection and 21 an IL injection. The IL and TF participant groups were very similar with respect to age, sex, and level of injections (Table 2 and 3) Four participants did not complete the study, with reasons ranging from loss to follow-up (not returning after steroid injection) to pursuing exclusion criteria items in Table 4. Thirty-eight participants were included in the final analysis, consisting of 18 in the IL group and 20 in the TF group (Fig. 1). Due to random chance, there was a slightly higher proportion of female participants in the TF group. As per the inclusion criteria, the most common radicular pain source diagnosis was intervertebral disc herniation. It accounted for all participants in the IL group and 19 of 20 participants in the TF group. In the TF group, one participant's radicular pain was clinically diagnosed to be from degenerative annular changes alone. Prior to the intervention, straight leg raise was positive in 17 of 18 participants in the IL group (average angle 45° ± 13.7 standard deviation [SD]). In the TF group, straight leg raise was positive in 17 of 20 participants (38° ± 15.9 SD). Regardless of the approach, the initial injection was highly successful in the majority of participants (defined as participant report of 75% relief). Only 3 out of the 18 participants in the IL group required a second repeat injection; among them 2 then received a crossover TF injection. After crossover, those 2 participants still did not experience relief of > 75%, nor subjective satisfaction. In the TF group, only 1 out of 20 participants was given a repeat injection and none crossed over to IL injection.

Overall, both the IL and TF techniques produced similar clinically significant improvements in pain, function, and depression assays. In the primary outcome measures, the follow-up pain NRS was more greatly reduced in the TF group; this was statistically significant in the 2-sided t test, P value < 0.05. Pain NRS decreased from 7.0 ± 1.9 to 3.9 ± 3.1 in the IL group and 6.4 ± 2.1 to 1.7 ± 1.4 in the TF group (Fig. 2A). The ODI was re-

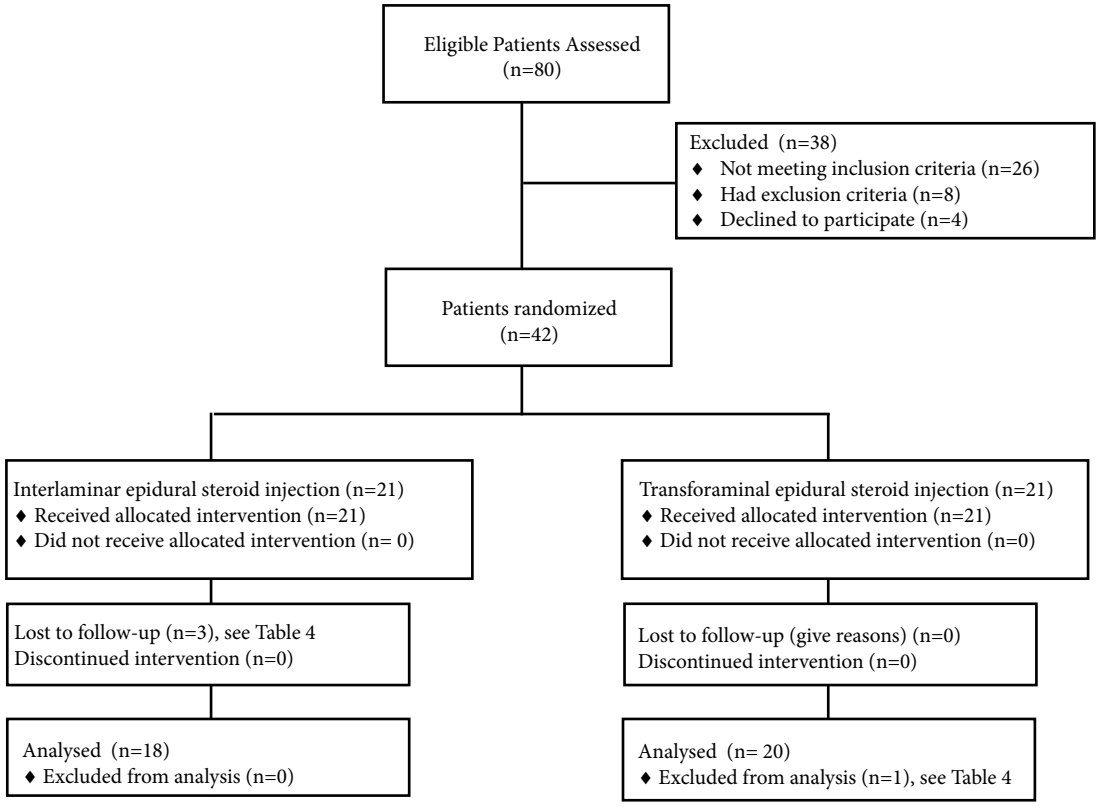

Fig. 1. *Study design and participant flow chart*

Table 2. *Demographic information for interlaminar steroid study patients*

Patient	Age	Gender	Injection Lefel	# of Injections
1727	26	male	L4-L5: right	1
9327	60	male	L4-L5: left	1
4028	31	male	L5-S1: left	1
7527	39	male	L5-S1: right	1
8927	62	male	L5-S1: right	2
3228	45	male	L5-S1: left	1
6928	39	male	L4-L5: right	1
1427	60	male	L5-S1: right	1
7827	85	male	L5-S1: left	1
8727	76	male	L5-S1: left	3- crossover
2127	47	female	L4-L5: right	1
4828	62	male	L5-S1: right	1
4228	71	female	L5-S1: right	3- crossover
7428	34	female	L5-S1: left	1
7128	40	male	L2-L3: left	1
7328	37	female	L5-S1: right	1
8628	40	female	L4-L5: left	1
1328	68	male	L5-S1: left	1

Crossover: if a 3rd injection was required, patients were crossed to the alternative injection technique

Table 3. *Demographic information for transforaminal steroid study patients*

Patient	Age	Gender	Injection Level	# of injections
1327	58	female	L4, L5: right	1
4228	54	male	L4, L5: left	1
1228	34	female	L4, L5: right	1
1227	52	male	L4, L5: right	1
7827	62	female	L4, L5: right	1
1027	61	male	L3, L4: right	2
5528	43	male	L4, L5: left	1
2528	36	male	L4, L5: right	1
1327	41	female	L4, L5: left	1
7728	69	male	L4, L5: left	1
8227	74	female	L4, L5: left	1
1127	34	male	L5, S1: right	1
7627	51	male	L5, S1: left	1
8727	31	female	L4, L5: right	1
4928	59	male	L5, S1: left	1
1527	35	female	L5, S1: left	1
8127	40	female	L4, L5: left	1
7228	39	female	L4, L5: right	1
1328	45	male	L4, L5: right	1
5428	42	male	L4, L5: left	1

Table 4. *Demographic information for patients excluded during the study*

Patient	Age	Gender	Injection Level	# of Injections	Reason Lost from Study
1927	64	female	IL: L3-L4	1	did not return for follow-up, reported excellent relief via phone
3727	42	female	IL: L5-S1	1	did not return for follow-up, reported excellent relief via phone
2527	51	female	IL: L4-L5	1	did not return for follow-up, reported 100% pain relief via phone
4328	26	male	TF: L4,L5 right	3	Injection protocol violation, another injection outside of ESI

duced from 37.5 ± 12.6 (mean values ± standard deviation) to 19.0 ± 16.7 in the IL group and 38.3 ± 6.4 to 21.6 ± 16.8 in the TF group (Fig. 2B). ODI and NRS regression plots failed to generate a correlation for both groups (Fig. 3).

In secondary outcomes, the depression scale was reduced from 4.4 ± 3.2 to 2.2 ± 3.2 in the IL group and 4.1 ± 1.9 to 1.7 ± 1.6 in the TF group (Fig. 4A). Walking tolerance was increased from 8.1 ± 4.6 blocks to 10.6 ± 4.4 in the IL group and 8.9 ± 5.3 blocks to 11.8 ± 4.2 in the TF group (Fig. 4B). All of the above changes in mean values after injection were statistically significant in the 2-sided t test, except for the walking tolerance in the TF group, which was significant for the one-tailed

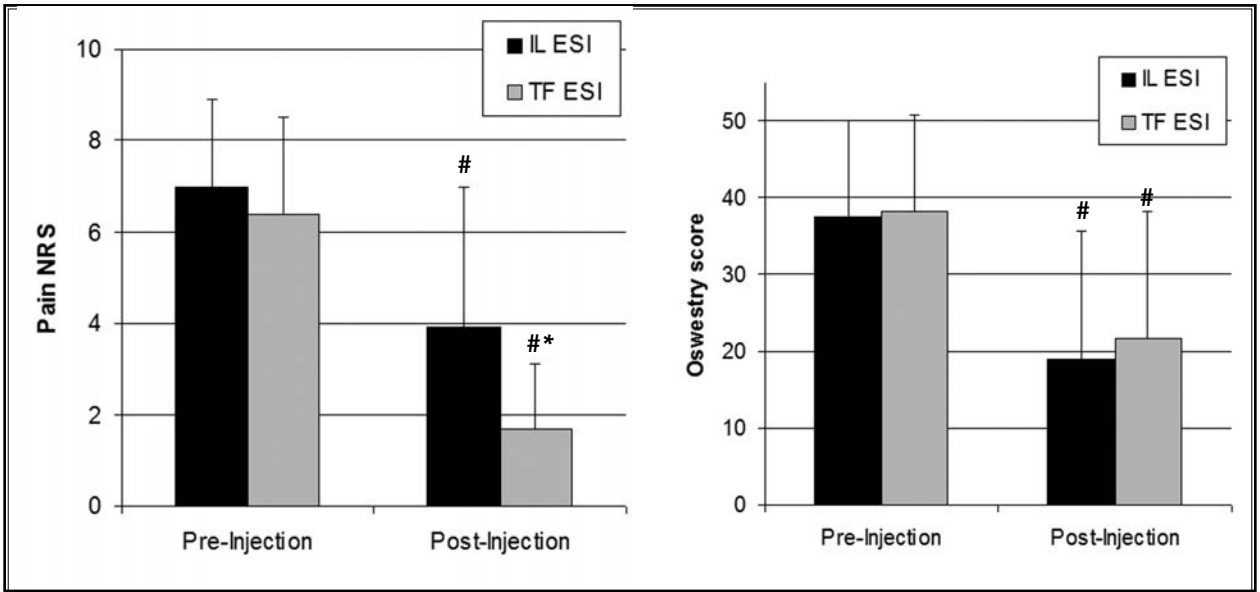

*Fig. 2. Pain numerical rating scale (A) and Oswestry Disability Index score (B) pre-ESI and 10-16 days post ESI. # represent significant difference using a 2-tailed t test compared to pre-injection levels in respective ESI. * represents significant difference using a 2-tailed t test comparing ESI injection types to each other. Results were considered statically significant if the P value was less than 0.05.*

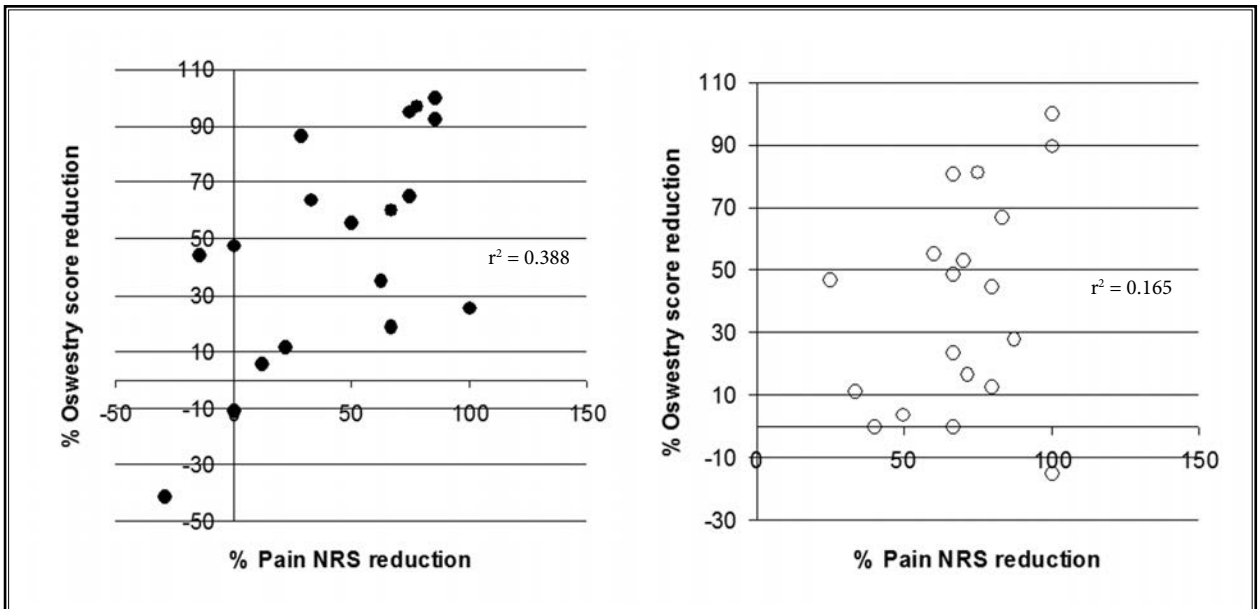

Fig. 3. Correlation of pain numerical rating scale and Oswestry Disability Index score. Black dots represent IL ESI (A) and white dotes represent TF ESI (B).

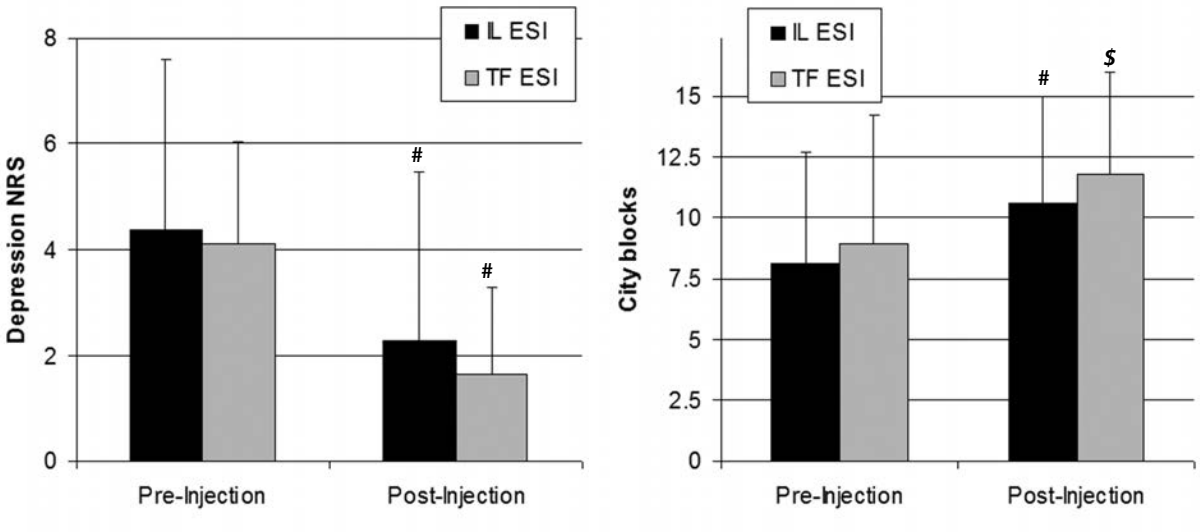

Fig. 4. *Depression numerical rating scale (A) and city block walking tolerance (B) pre-ESI and 10-16 days post ESI. # represent significant difference using a 2-tailed t test compared to pre-injection levels in respective ESI. $ represent significant difference using a one-tailed t test compared to pre-injection levels in respective ESI. Results were considered statically significant if the P value was less than 0.05*

t test. Prior to injection, 7 participants in the IL group took an average of 4.3 ± 3.40 opioid pills per day; after injection they averaged 1.3 ± 1.11 opioid pills per day (one had stopped use, one initiated). Prior to injection, 10 participants in the TF group took an average of 3.3 ± 1.89 opioid pills per day; after injection they averaged 1.1 ± 1.64 opioid pills per day (5 had stopped use, 2 initiated). In the IL group, 14 participants were in physical therapy prior to injection. Their tolerance to physical therapy (10 being intolerable, 0 being totally tolerable) was 3.4 ± 3.54; after injection, 1.8 ± 2.62 (one stopped physical therapy). In the TF group, 13 participants were in physical therapy prior to injection. Their tolerance to physical therapy was 5.0 ± 2.58; after injection, 1.4 ± 2.10. One TF patient stopped physical therapy, but 2 started after injection. Opioid pill use and physical therapy tolerance are summarized in Table 3. Statistics were not applied to the opioid pill use and physical therapy tolerance rating due to the smaller subpopulation of participants and changing "n" value of participants pre- and post-injection.

To summarize, improvements in percentage reduction across the different parameters between the 2 approaches were quite comparable. When examined with the 2-sided t test, only the reduction in pain NRS was statistically significant in favor of the TF group, while the rest of the parameters did not show a statistically significant difference between the interlaminar and transforaminal ESI groups.

Discussion

Lower back pain with radicular symptoms that correlate clinically to exam and imaging is an efficacious target for lumbar ESI in short-term pain management (15,20,23). Recent studies have compared IL and TF techniques in prospective trials. In a prospective, blinded and randomized, IL versus TF subacute low back axial pain study (no radiculopathy), both techniques had an approximately 50% reduction in pain scores and no difference was seen between the techniques (31). Smith et al (30) 2010 found that both IL and TF ESI injections similarly improved pain NRS in spinal stenosis, also with no difference in those requiring repeat injections or going onto surgery. While previous studies suggest ESI efficacy for axial low back pain and spinal stenosis (6,8,16,30,31,33,36,37), ESI for treatment of low back pain with radiculopathy is more accepted (5,6,8-17). Ackerman et al (23) focused on the anatomical location of epidural steroid placement, and in 6 through 24 week outcomes, demonstrated that pain NRS was more greatly reduced at 2 weeks with TF ESI compared to IL (approximately 35% lower mean values, reaching statistical significance). Oswestry scores and depression scales had similar improvements at 2 weeks for both techniques. While well done, this study was limited

to a single pathology level and all participants were under 60 years of age.

In the current study, we prospectively compared TF and IL ESI in the most accepted, validated, clinical scenario: acute pain relief in subacute radicular low back pain. Randomized patients, the assessment clinician, and the injection clinician were all blinded as outlined in the above methods, and the study included participants aged 26 to 85 with lumbar pathology from L2 to S1 (Tables 2 and 3). While the average age was very similar between the IL and TF groups, there were more women in the TF group (due to differential drop out, Table 4) however the subgroup analysis did not suggest a differential sex effect. The majority of participants in the study benefited clinically, regardless of the injection type. Collectively, 90% of the participants achieved 75% relief or subjective satisfaction after one ESI; only 4 participants required a repeat injection. This overall benefit is greater than that seen in previous studies and likely due to several factors, including injection level with strong correlation to exam (90% of the participants had associated positive straight leg raise); clinical history, imaging, and radicular pain etiology (all but one had an intervertebral disc herniation that directly correlated with symptoms); the experience of the injecting practitioner; and ipsilateral targeting of IL injections.

While long-term outcomes focus on surgery, return to work, and financial consideration, short-term outcomes have focused on patient relief, numerical pain score, disability, and functional assessment (13-17,23). As such, primary outcome measures were the pain NRS and the ODI. Pain NRS was lowered more significantly in TF ESI than IL; there was a 44% reduction after IL ESI versus 74% after TF ESI (Fig. 2A). These results are similar to those reported by Ackerman et al (23) in 2007, where IL ESI reduced pain NRS by 35%, and TF ESI by 82%. With respect to ODI, post IL and TF ESI, ODI was reduced approximately 50% (Fig. 2B). Both injection types produced clinically and statistically significant results, but no difference was seen between the 2 injection types. Ackerman et al (23) found nearly identical ODI reductions, with no difference between TF and IL ESI. However, their participant population was younger, with a mean age of 36.5 years (the current study mean age was 49.8 years) and only explored L5-S1 pathology. Though the methodology for the 2 studies was not identical, both compared IL ESI and TF ESI for lumbosacral radicular low back pain approximately 2 weeks after injection. In the current study, while both ODI and pain NRS improved after ESI; no correlation between ODI and pain NRS was seen for either injection type (Fig. 3). The disassociation of pain NRS and the participant's self-functional assessment has been seen previously (49-51). It is possible that a correlation may have been appreciated with 200 participants per study arm, but one would question the clinical significance of such a correlation for a procedure based therapy.

In secondary outcomes, an equal benefit for both IL and TF ESI was demonstrated across parameters with striking similarity. Both IL and TF depression NRS was reduced approximately 50%, while both increased walking tolerance approximately 30% (Fig. 4). Only 17 participants in the study were using opioid analgesics. Across both IL and TF groups, opioid pill use was reduced a mean 2-3 pills per day after ESI (Table 5). Friendly et al (49) In 2008, suggested that opioid pill use was not decreased after ESI for lower back pain. The likely reason for this difference was the high pretest probability of participant success with ESI in our study. All participants in the current study had subacute radicular low back pain, where exam and imaging matched clinical history. Friendly et al's (49) data were retrospective with various low back etiologies, including nonspecific low back pain and spinal stenosis where ESI is thought to be less effective. Lastly, the current study demonstrated tolerance to physical therapy increased (more able to tolerate) across both injection types 50-70%, but only 27 participants were enrolled in physical therapy prior to ESI. Due to the low number of participants

Table 5. *Opioid use and tolerance to physical therapy*

	Opioid Use		Tolerance to Physicial Therapy	
	Transforaminal	Interlaminar	Transformaminal	Interlaminar
Patients using, or enrolled, prior to ESI	10	7	13	14
Pills used, or score reported, prior to ESI	3.3 ± 1.89	4.3 ± 3.40	5.0 ± 2.58	3.4 ± 3.54
Pills used, or score reported, after ESI	1.1 ± 1.64	1.3 1.11	1.4 ± 2.10	1.8 ± 2.62
Patients using, or enrolled, after ESI	7	7	14	13

and established wide clinical variability, statistics were not applied to opioid pill use and tolerance to physical therapy data.

The limitations of this study include sample size, lack of long-term and nonclinical end points, and that a single practitioner performed all ESIs. While a statistical difference for pain NRS comparing TF and IL ESI was found, it is possible a larger sample size could see differences for other primary and secondary outcomes. However, other than pain NRS, no separation trends were seen, and one would question the clinical application of very large studies to show very small outcome differences. Long-term and nonclinical outcomes (such as economics and number of participants going on to surgery) were not explored in the current study. These would be interesting results to pursue in a subsequent clinical trial. Lastly, since a single experienced interventionalist performed all injections, this may have increased efficacy and decreased outcome variability.

The participants were novices to the different injection experiences, therefore optimizing the participant blinding. They saw their procedure as "an injection" or an "epidural steroid injection." The interval in which the 2 TF needles broke the skin were seconds apart. While highly experienced patients receiving injections would likely know the difference, we believe our participant population was not likely to.

In summary, this study compared the clinical effectiveness of IL and TF ESI in subacute low back pain with radiculopathy. TF ESI lowered pain NRS more than IL ESI, a finding similar to previous studies (22,23). However, this was the only difference seen between the 2 techniques. All assays of disability, function, depression, and opioid use showed no difference between the techniques, with both IL and TF ESI being very effective. More than 90% of all participants achieved 75% relief or subjective satisfaction after one injection, regardless of type. This is likely due to only including participants with high pretest probability for success, as previously stated. Secondly, IL techniques may have outperformed previous studies due to a lateral parasagittal interlaminar approach (leftward or right, toward the side of complaint) compared to a traditional midline approach (29). TF ESI represents significantly higher risks of adverse events to the patient, including a 10-fold higher incidence of intradiscal injection (thus higher risk of discitis) and a possible spinal cord infarct (52,53). While the probability of spinal cord conus infarct is remote with TF ESI in the lumbar spine, it is devastating to the patient when it happens (53-59). To our knowledge, there have only been 2 case reports of spinal cord infarct, MRI confirmed, with lumbar IL ESI (60-61). In both cases, the patient had prior spine surgery at the level of IL ESI. Likely, post-surgical changes in the epidural space and arterial spinal vasculature contributed to the spinal cord infarcts with IL ESI done at the surgical level. There has never been a reported spinal cord infarct with IL ESI on a patient that did not have prior spinal surgery at the same IL level. While complications rarely occur with ESI at any level, drastic poor outcome (paralysis and death) appears more likely to occur at cervical levels and with TF approaches (62-79).

Conclusion

Considering the equal functional benefit from both IL and TF techniques in this prospective, blinded study and the preferred safety profile and less patient discomfort associated with IL ESI injections, the initial ESI technique of choice may favor IL injections even though TF ESI appears to reduce acute pain NRS more significantly. If there is inadequate relief after 2 weeks with the IL ESI, then TF ESI can be considered at that point in time.

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