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Original Research Article

Adverse Event Rates Associated with Transforaminal and Interlaminar Epidural Steroid Injections: A Multi-Institutional Study

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Abstract

Background. Transforaminal epidural steroid injections (TFESI) have demonstrated efficacy and effectiveness in treatment of radicular pain. Despite little evidence of efficacy/effectiveness, interlaminar epidural steroid injections (ILESI) are advocated by some as primary therapy for radicular pain due to purported greater safety.

Objective. To assess immediate and delayed adverse event rates of TFESI and ILESI injections at three academic medical centers utilizing International Spine Intervention Society practice guidelines.

Methods. Quality assurance databases from a Radiology and two physical medicine and rehabilitation (PM&R) practices were interrogated. Medical records were reviewed, verifying immediate and delayed adverse events.

Results. There were no immediate major adverse events of neurologic injury or hemorrhage in 16,638 consecutive procedures in all spine segments (14,956 TFESI; 1,682 ILESI). Vasovagal reactions occurred in 1.2% of procedures, more frequently ($P = 0.004$) in TFESI (1.3%) than ILESI (0.5%). Dural punctures occurred in 0.06% of procedures, more commonly after ILESI (0.2% vs 0.04%, $P = 0.006$). Delayed follow up on PM&R patients (92.5% and 78.5, next business day) and radiology patients (63.1%, 2 weeks) identified no major adverse events of neurologic injury, hemorrhage, or infection. There were no significant differences in delayed minor adverse event rates. Central steroid response (sleeplessness, flushing, nonpositional headache) was seen in 2.6% of both TFESI and ILESI patients. 2.1% of TFESI and 1.8% of ILESI patients reported increased pain. No long-term sequelae were seen from any immediate or delayed minor adverse event.

Conclusions. Both transforaminal and ILESI are safely performed with low immediate and delayed adverse event rates when informed by evidence-based procedural guidelines. By demonstrating comparable safety, this study suggests that the choice between ILESI and TFESIs can be based on documented efficacy and effectiveness and not driven by safety concerns.

Key Words. Epidural; Steroid; Radiculopathy

Introduction

Epidural steroid injections, particularly transforaminal epidural steroid injections (TFESI), have been portrayed as dangerous procedures in publications citing only isolated case reports. Case reports constitute very low

quality evidence, but have inappropriately been used to make practice recommendations for interventional spine procedures. A recent comprehensive review of epidural steroid injections suggested that interlaminar epidural steroid injections (ILESI) should be the initial injection technique in higher risk spinal segments (upper lumbar and cephalad) [1]. This recommendation is based on TFESI safety concerns, and occurs despite the paucity of efficacy data for the interlaminar approach, and the much higher quality literature supporting lumbar TFESI [2]. More egregious is the statement in another review article that "the multitude of risks attributed to these injections [epidural steroid injections] outweighs the benefits" [3]. A more rational approach is the study of Benny et al., who compiled reported complications of cervical TFESI, but acknowledged that the literature reviewed (case reports) was of too low quality to support practice recommendations [4].

The United States Food and Drug Administration safety alert of April 2014 stated that the "effectiveness and safety of injections of corticosteroids into the epidural space has not been established, and FDA has not approved corticosteroids for this use" [5]. However, lumbar TFESIs are supported by robust efficacy and effectiveness literature [2]. The context of this safety alert is important to consider. The FDA referenced primarily case reports, compilations of case reports and nonconsecutive retrospective series [5]. These studies provide no ability to understand the rate of adverse events related to these procedures. In addition to low quality methodology, the existing literature provides no control for the specific technique employed in performing TFESI or ILESI. Any surgical or minimally invasive procedure can be rendered dangerous by flawed technique.

A large consecutive series of prospectively acquired immediate and delayed follow-up data after transforaminal and ILESI performed with rigorous adherence to evidence-based guidelines is necessary to better understand the *rate* of associated adverse events when using best practices. That is the objective of this study.

Methods

This study was approved by the Institutional Review Boards of the parent institutions and complied with all Health Insurance Portability and Accountability Act requirements. The participating institutions were a radiology spine procedural practice at the Mayo Clinic (Mayo), and physical medicine and rehabilitation spine practices at the Northwestern University/Rehabilitation Institute of Chicago (RIC) and The University of Pennsylvania (Penn). There were a total of 16,638 consecutive epidural procedures performed in all spine segments. The Mayo study cohort was obtained by interrogation of a quality assurance database inclusive of January 1, 2006 through December 11, 2013. In this study period, 11,365 total epidural steroid injections were performed, including 9,963 TFESIs and 1,402 ILESIs. The RIC and Penn cohorts were obtained by interrogation of a discrete structured clinical database (RICPLAS©—Rehabilitation Institute of Chicago Physiatric Log & Analysis System). Procedures at RIC were performed between March 2004 and January 2009, consisting of 4,507 TFESIs and 280 ILESIs. At Penn, 486 TFESIs were performed from September 2009 through July 2010. Start and end dates of each study centers database reflect the dates that the teams were able to collect valid data on consecutive procedures and do not intentionally exclude significant adverse events. The time frames of the datasets were limited by institutional operational constraints rather than exclusion of poor outcomes. The tabulation of the injections performed by spine segment and study sample demographics are shown in Table 1.

All lumbar epidural injections were performed in accordance with ISIS guidelines [2]. Lumbar TFESIs and ILESIs were performed under fluoroscopic guidance; CT guidance was used in select Mayo cases (2.0%) when difficult anatomy, postoperative change or body habitus precluded a safe fluoroscopically guided injection. At Mayo, TFESIs were performed with 25-gauge spinal needles wherever possible; 22 gauge needles were

Table 1 Procedures and demographics

Institution	Total Cohort	Mayo	RIC	Penn
N Subjects	9,998	6,819	2,898	281
Gender (% female)	52.8	49.5	58.1	47.7
Age (mean ± SD)	58.3 ± 16.3	60.8 ± 15.7	52.9 ± 16.4	53.3 ± 15.4
N Procedures	16,638	11,365	4,787	486
Type:				
Interlaminar (%)	1,682	1402 (12.3)	280 (5.8)	0
Transforaminal (%)	14,956	9963 (87.7)	4,507 (94.2)	486 (100)
Segment:				
Cervical	1,450	966 (8.5)	404 (8.4)	80 (16.5)
Thoracic	228	196 (1.7)	30 (0.7)	2 (0.4)
Lumbosacral	14,960	10,203 (89.8)	4,353 (90.9)	404 (83.1)

used when additional needle length or stiffness was required. At RIC and Penn, 22 gauge spinal needles were primarily used. Contrast injection was always performed via extension tubing and observed under live fluoroscopy in the anterior–posterior (A–P) view to exclude intravascular flow. Epidural flow vs any abnormal flow pattern was verified in both anterior–posterior (A–P) and lateral planes at Mayo. At Penn and RIC, (A–P) views only were used for contrast injection under live fluoroscopy to identify epidural, intravascular, and other abnormal flow patterns. Following a satisfactory contrast injection, a test injection was performed with 1 cc of 2% lidocaine at Mayo and with 1.5–2 cc of 1% lidocaine at RIC and Penn. A one to two minute pause assured no cardiovascular or neurologic change had occurred in response to the test injection.

Over the study period, the corticosteroids used included triamcinolone acetonide (Kenalog, 80 mg in 2 mL, Bristol-Myers Squibb, New York, NY), betamethasone sodium phosphate/betamethasone acetate (Celestone, 12 mg in 2 mL, American Regent, Inc., Shirley, NY) or preservative free dexamethasone sodium phosphate (10 mg in 1 mL, APP Pharmaceuticals, LLC, Lake Zurich, IL). At all three institutions, Betamethasone was the preferred agent for TFESIs from 2004 to 2009; triamcinolone was used when betamethasone was not commercially available. In response to safety concerns [6] dexamethasone became the preferred corticosteroid for all Mayo lumbar TFESIs after October 2010 and all Penn TFESIs after August 2009. The anesthetic test injection and corticosteroid injection were executed via the distal end of the extension tube to avoid direct contact with the needle during syringe exchange.

At Mayo and RIC, ILESIs were performed with 20 gauge Tuohy needles. No ILESIs were performed at Penn during the study period. The dorsal epidural space was entered with loss of resistance technique. Contrast injection was always performed and viewed with live fluoroscopy in A–P and lateral planes to confirm epidural flow and exclude intravascular, subdural, or intrathecal flow. The corticosteroids used for lumbar ILESIs were betamethasone preferentially, and triamcinolone when betamethasone was unavailable, at the doses noted above.

Cervical and thoracic epidural injections at Mayo were performed with CT-fluoroscopic (CT/F) guidance. Mayo cervical TFESIs were performed via either an anterolateral or posterolateral approach with 25-gauge needles as has been previously described [7,8]. The ISIS Guidelines were replicated using CT/F guidance, with the added safety factor of direct visualization of vulnerable vascular or neural structures during needle placement and contrast, lidocaine and steroid injection. Multislice CT/F acquisitions during and following cessation of contrast injection were used to exclude vascular or intrathecal flow and assess epidural distribution. Fluoroscopic guidance without CT was used to guide cervical and thoracic epidural injections at RIC; 22 gauge needles were typically employed for TFESI. As in the lumbar spine, contrast injection was always performed under live fluoroscopic observation in the A–P plane, and observed in the ipsilateral oblique plane, to confirm an epidural distribution and exclude intravascular, subdural, or intrathecal flow. Confirmation of an appropriate flow pattern was followed by a lidocaine test injection (1 cc of 2% lidocaine or 0.5 cc of 4% lidocaine at Mayo and 1 cc of 1% lidocaine at RIC and Penn) followed by a 1-minute pause. Subsequently, 10–13 mg of dexamethasone was injected. Cervical and thoracic ILESIs were also performed with CT/F guidance at Mayo and fluoroscopic guidance alone at RIC and Penn using 20 gauge Touhy needles, loss of resistance technique to enter the dorsal epidural space, followed by contrast injection during CT/F imaging or live fluoroscopic or digital subtraction imaging in the AP plane. At Penn and RIC, the contrast spread pattern was also confirmed by observation in the lateral or contralateral oblique planes. Betamethasone or dexamethasone were used for interlaminar injections.

Conscious sedation was rarely used for epidural injections in any spine segment. The previously reported sedation rate for Mayo TFESIs was 0.1% [9]. No patients were sedated at Penn. At RIC, 4.5% of all epidural injection patients were given mild intravenous sedation, in which the patient remained conversant. Nursing personnel who were skilled in distraction and empathetic interaction attended all patients throughout the procedures. Nursing personnel monitored patients for approximately 30 minutes after the procedure; they were then evaluated by the treating physician (Mayo) or either a physician or nursing personnel (RIC, Penn) prior to dismissal, after meeting safe discharge criteria.

The treating physician directly entered immediate adverse events into the respective databases at the three institutions (Table 2). At RIC and Penn, to assure accuracy, all procedural data were entered via a drop down menu and free text in the electronic clinical database by the treating physician. Additional adverse events could also be entered into the clinical database immediately by nurses in the postprocedure recovery area. Persistent leg/arm weakness was considered to be any permanent neurologic injury. Vasovagal reactions were defined as signs (bradycardia, hypotension, and diaphoresis) and/or symptoms (nausea or lightheadedness) reflective of increased vagal/decreased sympathetic tone. For vasovagal reactions, the medical record was reviewed for interventions that were required. Allergic reactions were defined as signs (hives, erythema) or symptoms (shortness of breath requiring intervention indicating bronchospasm or laryngeal edema) characteristic of a contrast reaction. The cause of each aborted procedure was reviewed. In addition, a search was performed for Emergency Department (ED) visits that occurred up to 2 days after each procedure.

Delayed adverse events were captured by telephone query from a paramedical assessor independent of the treating physician. This assessor was not involved in

Table 2 Potential adverse events evaluated

Immediate Adverse Events	Delayed Adverse Events
Persistent leg or arm weakness requiring imaging or intervention	Neurological deficit
Hemorrhage requiring imaging or intervention	Hemorrhage
ED transfer	Infection
ED visit within 48 hours	Increased pain
Vasovagal reaction	Increased pain; complication identified
Vasovagal reaction, aborted procedure	Central steroid effect
Aborted procedures	Allergic reaction
Allergic reaction	CSF leak/spinal headache
Dural puncture	Diabetic complications

data analysis. The delayed query occurred the next business day (24–72 hours) at RIC and Penn, and at two weeks postprocedure at Mayo. This interview included both outcome measures and a scripted series of questions regarding potential complications (Table 2). The RIC and Penn scripted questions included a more granular description of symptoms experienced; the symptoms were combined into groupings to match the more categorical descriptions of complications scripted in the Mayo follow up. New or increased weakness was defined as a documented motor deficit that arose subsequent to the injection. Increased pain was defined as documented increased pain in a radicular distribution attributable to the injection procedure. Hemorrhagic complications included any reported bleeding requiring imaging or intervention. Allergic reactions are defined above. CSF leak was defined as a postural headache requiring treatment, inclusive of but not restricted to supine bed rest and a blood patch. Infectious complications included any documented deep or superficial infection. Central steroid response was defined as facial flushing, nonpositional headache, sleeplessness, or agitation that was self-limiting.

The databases were interrogated for all immediate postprocedure adverse events at all three institutions and at 24–72 hours for RIC and Penn and at 2 weeks at Mayo. The electronic medical record (EMR) was then reviewed on all positive responses to verify or refute the presence of an adverse event and ascertain its causal relationship to the procedure. Virtually all patients (>99%) had documented clinical follow up that allowed verification. The only complication categories which were not reviewed were: 1) the presence of transient weakness immediately after a TFESI, where motor blockade was expected, and 2) symptoms of central steroid effect (flushing, nonpositional headache, sleeplessness), as there would not likely be data to verify or refute the response given to the paramedical assessor.

Logistic regression models were used to examine the difference in various complication rates by injection type. Complication (yes/no) was defined as the outcome, and type of injection (interlaminar/transforaminal) was used as the predictor in each model.

Complication percentages by procedure type are included rather than odds ratios for ease of interpretation and to better illustrate the context of the frequencies of each complication.

Results

The demographics of the study cohort are presented in Table 1. Sixteen thousand six hundred and thirty eight epidural procedures were performed; 89% were TFESIs and 89% were performed in the lumbosacral spinal segments. Mayo contributed 69% of the cases; the Mayo population was older than that seen at RIC and Penn. The adverse events recorded are noted in Table 2, with definitions detailed in the methods section above. Complete data on immediate and delayed adverse events segregated by spine segment for each institution are included in the Appendix.

Immediate Adverse Events

Table 3 enumerates immediate adverse events noted at the time of the procedure. There were no persistent neurologic deficits following any procedure. Transient motor blockade, an expected finding following TFESI, is not an adverse event; this was seen in 19% of TFESIs in an earlier study of the Mayo cohort [10]. There were no recorded falls or injuries associated with transient motor blockade. No hemorrhagic events occurred following either TFESI or ILESI.

Six patients (0.04%) were transferred to an emergency department following TFESI at Mayo; two complained of chest pain (subsequently dismissed with negative troponins), three exhibited atypical allergic reactions with a respiratory component (all were determined to be psychogenic reactions) and one complained of increased leg pain, which resolved. Presentation to an emergency department within 48 hours was noted in 0.05% of patients (0.04% of TFESIs and 0.1% of ILESIs). TFESI patients presented with increased pain (0.03%, $n = 4$), allergic reactions (0.01%, $n = 2$) or nonpostural headache (0.006%, $n = 1$); 0.1% ($n = 2$) of ILESI patients presented with increased pain. There were no sequelae associated with any of the emergency department transfers or later presentations.

Vasovagal reactions occurred in 1.3% of TFESI and 0.5% of ILESI; they resulted in aborted procedures in 0.2% of TFESIs. Among the 35 Mayo vasovagal

Table 3 Immediate and delayed adverse events, all sites by procedure type

	Total N = 16,638	Interlaminar N = 1,682	Transforaminal N = 14,956
Immediate Adverse Events			
Persistent weakness	0	0	0
Hemorrhage	0	0	0
ED transfer	6 (<0.1)	0	6 (<0.1)
ED visit within 48 hours	9 (<0.1)	2 (0.1)	7 (<0.1)
Vasovagal reaction	208 (1.2)	8 (0.5)	200 (1.3)
Vasovagal reaction-abort	36 (0.2)	0	36 (0.2)
Aborted procedures	127 (0.8)	6 (0.4)	120 (0.8)
Allergic reaction	8 (<0.1)	0	8 (<0.1)
Dural puncture	10 (<0.1)	4 (0.2)	6 (<0.1)
Delayed Adverse Events			
Neurologic deficit	0	0	0
Hemorrhage	0	0	0
Infection	0	0	0
Increased pain	357 (2.1)	30 (1.8)	327 (2.1)
Increased pain complication identified	0	0	0
Central steroid effect	428 (2.6)	43 (2.6)	385 (2.6)
Allergic reaction	13 (<0.1)	1 (<0.1)	12 (<0.1)
CSF leak/spinal headache	6 (<0.1)	1 (<0.1)	5 (<0.1)
Diabetic complication	11 (<0.1)	1 (<0.1)	10 (<0.1)

reactions, only four required intravenous fluids; the remainder responded to tredelenburg positioning, oxygen, and reassurance. Procedures at all sites were aborted in 0.8% of TFESI and 0.4% of ILESI. Vasovagal reactions were the most common reason for aborted TFESI (0.24%, n = 36), followed by pain (0.17%, n = 26), and persistent intravascular flow (0.16%, n = 22). Intrathecal filling was the most common cause of aborted ILESI procedures (0.18%, n = 3). Allergic reactions occurred in <0.1% of TFESI patients. Dural punctures were detected in 0.2% of ILESIs and <0.1% of TFESIs.

Immediate adverse events are segregated by spine segment in Table 4. Aborted procedures occurred at a slightly higher rate in cervicothoracic compared with lumbosacral procedures. In lumbosacral procedures, vasovagal reactions were more frequent with TFESI than ILESI; this was reversed in the cervicothoracic segment, where vasovagal reactions were more common with ILESI.

Logistic regression models (Table 6) examined the difference in rates of immediate adverse events for TFESI and ILESI. The rate of vasovagal reactions for TFESI was higher than that seen with ILESI ($P = 0.004$). The rate of observed dural punctures was higher with ILESI than TFESI ($P = 0.006$). There was no significant difference between TFESI and ILESI in other rates of immediate adverse events. The difference in rate of aborted procedures (TFESI > ILESI) approached statistical significance ($P = 0.0524$).

Delayed Adverse Events

There were no cases of fixed neurologic deficit, intraspinal/paraspinal hemorrhage, or infection following any TFESI or ILESI (Table 3). Increased pain was reported on delayed follow up in 2.1% of TFESI and 1.8% of ILESI patients. The EMR was examined in all of these patients; no procedure related sequelae were identified.

The Mayo cohort noted increased pain in response to a scripted query at 2 weeks postprocedure in 2.1% of patients (2.1% TFESI, n = 211; 1.9% ILESI, n = 26). Comparison with preprocedure pain scores showed that of these 237 patients, only 9% or 22 patients (0.2% TFESI, n = 21; 0.07% ILESI, n = 1) actually reported a higher pain score at 2 weeks than baseline. The response to the scripted query about increased pain may reflect failure to meet expectations of pain relief rather than worsened pain. Review of the Mayo EMR identified 0.26% of TFESI patients (n = 26) with physician visits citing increased pain. These complaints provoked MRI imaging in 11 cases. There were six patients with progression of disc herniation or foraminal compromise; there were no cases of infection, hemorrhage or procedure related complication. 0.21% of ILESI patients (n = 3) had physician visits citing increased pain; one case underwent negative MRI imaging. There were no cases of long term sequelae identified at any of the study sites among patients who reported increased pain on delayed follow up.

Central steroid effects, consisting variably of flushing, agitation, sleeplessness or nonpostural headache,

Table 4 Immediate adverse events at all sites by spine segment

	Total N = 14,960	Interlaminar N = 1,412	Transforaminal N = 13,548
Lumbosacral			
Persistent weakness	0	0	0
Hemorrhage	0	0	0
ED transfers	5 (<0.1)	0	5 (<0.1)
ED visits within 48 hours	9 (<0.1)	2 (0.1)	7 (<0.1)
Vasovagal reaction	192 (1.3)	3 (0.2)	189 (1.4)
Vasovagal-abort	34 (0.2)	0	34 (0.3)
Aborted procedures	108 (0.7)	5 (0.4)	103 (0.8)
Allergic reaction	8 (<0.1)	0	8 (<0.1)
Dural punctures	10 (<0.1)	4 (0.3)	6 (<0.1)
Cervicothoracic	N = 1,678	N = 270	N = 1,408
Persistent weakness	0	0	0
Hemorrhage	0	0	0
ED transfers	1 (<0.1)	0	1 (<0.1)
ED visits within 48 hours	0	0	0
Vasovagal reaction	16 (1.0)	5 (1.9)	11 (0.8)
Vasovagal-abort	2 (0.1)	0	2 (0.1)
Aborted procedures	19 (1.1)	2 (0.7)	17 (1.2)
Allergic reaction	0	0	0
Dural punctures	0	0	0

Table 5 Delayed adverse events at all sites by spine segment

	Total N = 14,960	Interlaminar N = 1,412	Transforaminal N = 13,548
Lumbosacral			
Neurologic deficit	0	0	0
Hemorrhage	0	0	0
Infection	0	0	0
Increased pain	324 (2.2)	23 (1.6)	301 (2.2)
Complication identified	0	0	0
Central steroid effect	400 (2.7)	36 (2.5)	364 (2.7)
Allergic reaction	10 (<0.1)	1 (<0.1)	9 (<0.1)
CSF leak/spinal headache	6 (<0.1)	1 (0.1)	5 (<0.1)
Diabetic complication	11 (<0.1)	1 (<0.1)	10 (<0.1)
Cervicothoracic	N = 1,678	N = 270	N = 1,408
Neurologic deficit	0	0	0
Hemorrhage	0	0	0
Infection	0	0	0
Increased pain	33 (2.0)	7 (2.6)	26 (1.8)
Complication identified	0	0	0
Central steroid effect	28 (1.7)	7 (2.6)	21 (1.5)
Allergic reaction	2 (0.1)	0	2 (0.1)
CSF leak/spinal headache	0	0	0
Diabetic complication	0	0	0

occurred in 2.6% of TFESIs and ILESIs. Delayed manifestations of allergic reactions, CSF leak/spinal headache, or diabetic complications occurred in <0.1% of TFESIs or ILESIs. Although delayed allergic reactions were rare and generally consisted of rashes, one delayed anaphylactoid reaction was observed, attributed to iodinated contrast material. It should be noted that diabetic complications were not specifically addressed

Table 6 Rates of adverse events by procedure type

	Total N = 16,638	Interlaminar N = 1682	Transforaminal N = 14,956	*P* Value
Immediate				
Persistent weakness	0	0	0	—
Hemorrhage	0	0	0	—
ED transfer	6 (<0.1)	0	6 (<0.1)	0.9920
ED visit within 48 hours	9 (<0.1)	2 (0.1)	7 (<0.1)	0.2439
Vasovagal reaction	208 (1.2)	8 (0.5)	200 (1.3)	0.0040
Vasovagal-abort	36 (0.2)	0	36 (0.2)	0.9873
Aborted procedures	126 (0.8)	6 (0.4)	120 (0.8)	0.0524
Allergic reaction	8 (<0.1)	0	8 (<0.1)	0.9908
Dural puncture	10 (<0.1)	4 (0.2)	6 (<0.1)	0.0058
Delayed	N = 16,638	N = 1,682	N = 14,956	*P* value
Neurologic deficit	0	0	0	—
Hemorrhage	0	0	0	—
Infection	0	0	0	—
Increased pain	357 (2.1)	30 (1.8)	327 (2.1)	0.2849
Complication found	0	0	0	—
Central steroid effect	428 (2.6)	43 (2.6)	385 (2.6)	0.9740
Allergic reaction	13 (<0.1)	1 (<0.1)	12 (<0.1)	0.7749
CSF leak/spinal HA	6 (<0.1)	1 (<0.1)	5 (<0.1)	0.5980
Diabetic complication	11 (<0.1)	1 (<0.1)	10 (<0.1)	0.9121

in the scripted queries, but were uncovered in evaluation of EMR follow up, and may be underestimated.

Delayed adverse events are segregated by spine segment in Table 5. Increased pain occurred at a slightly higher rate in TFESI than ILESI in the lumbosacral segments; in the cervicothoracic segments increased pain was more common after ILESI. Central steroid effects were slightly more frequent following ILESI in the cervicothoracic segments.

Logistic regression models identified no significant differences in rates of delayed adverse reaction between TFESI and ILESI (Table 6).

Discussion

This study demonstrates that both TFESI and ILESI are safe procedures when informed by the evidence-based guidelines of the International Spine Intervention Society. Prospectively collected data on over 16,000 consecutive epidural procedures at three institutions with practices based in two different medical specialties revealed no major adverse events, including neurologic injury, hemorrhagic event, or infection. Minor adverse events of vasovagal reaction occurred more frequently in TFESI, while dural punctures were identified more commonly in ILESI. Rates of other immediate adverse events (aborted procedures, ED transfers, ED visits, allergic reactions) or delayed adverse events (increased pain, central steroid effects, delayed allergic reactions, spinal headache, or diabetic complications) were indistinguishable between TFESI and ILESI. There were no negative sequelae from the identified minor adverse events on review of the EMRs of those patients.

The safety of both TFESI and ILESI demonstrated in this study is in concert with the existing reports of smaller controlled trials that primarily assessed the effectiveness of these procedures, and other larger observational trials assessing adverse events. No serious infectious or neurologic complications have been documented in any controlled or prospective observational study of either TFESI or ILESI to our knowledge. Among controlled trials, the only hemorrhagic complication reported was a retroperitoneal hematoma in a patient undergoing TFESI while on anticoagulants [11].

Among larger observational studies, where rates of adverse events can be calculated, a retrospective study reviewed 4,265 TFESI and ILESI in all spine segments over a 7-year period in a single academic physiatry practice [12]. There were no serious adverse events; minor adverse events occurred at a rate of 2.4%, more commonly with ILESI (6%) than TFESI (2.1%). Increased pain was the most common minor adverse event [12]. A prospective study of 1,305 lumbar TFESIs performed in 562 patients over a 5-year period in an academic anesthesiology practice recorded no serious adverse events [13]. Minor adverse events occurred in 11.5%, most commonly vasovagal reactions [13]. Another prospective study of 5,437 TFESIs and ILESIs performed in a private practice setting over a 20 month period noted no major adverse events of neurologic injury, intraspinal hemorrhage, or infection [14]. Minor adverse events were recorded in 3.2%. The most common minor adverse event was transient nerve root irritation,

seen in 4.6% of lumbar TFESIs. A private practice physiatry group contributed retrospective case series of lumbar TFESI [15] and cervical ILESI [16]. In the lumbar TFESI study, 227 patients underwent 322 injections; no major adverse events were seen. Minor adverse events were seen in 9.6%, most commonly central steroid effects [15]. In the cervical study, 157 patients received 345 ILESIs; no major adverse events were seen, although minor adverse events occurred in 16.8%. The most common minor adverse events were increased pain and central steroid effects [16]. There were no sequelae from the minor adverse events in either study.

Serious adverse events are very rare in either TFESI or ILESI. This contradicts the erroneous impression that can arise from examination of case reports alone. Minor adverse events are also very uncommon, and seldom or never lead to long-term sequelae. The rates of minor adverse events are difficult to compare given varying definitions of this category, but there is no clear pattern favoring either TFESI or ILESI. With comparable safety, the decision regarding the technique of delivery of corticosteroids should be driven by efficacy and effectiveness data, which strongly favors the transforaminal approach [2].

This study has weaknesses. All of the study data were collected prospectively, but immediate adverse events may be missed if the performing physician failed to properly note the event in the clinical database (Penn, RIC) or quality assurance database (Mayo). Delayed adverse events were collected at two time points, the next business day (24–72 hours postprocedure) at RIC and Penn vs 2 weeks for Mayo. Complications requiring additional time to manifest may have been missed in the earlier collection of delayed adverse events; however, rates of delayed complications did not substantively differ between Mayo and the other sites. The follow up was incomplete, with successful queries for delayed adverse events occurring in 92.5% of RIC patients, 78.5% of Penn patients, and 63.1% of Mayo patients. These numbers simply reflect insufficient resources to obtain follow up contact with every procedural patient, but do create an opportunity for bias. As for strengths, this study cohort represents the largest assemblage of prospective data on consecutive epidural steroid injection patients to date, recording no major adverse events.

Conclusion

Epidural steroid injections are safely performed by either the transforaminal or interlaminar technique when evidence-based practice guidelines are used. No major adverse events were seen in more than 16,000 consecutive procedures. Selection of the injection route should be based on relative efficacy and effectiveness data, not safety considerations.

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Appendix

Table A1 Immediate adverse events, Mayo: lumbosacral

Adverse Event	Total N = 10,203	ILESI N = 1,292	TFESI N = 8,911
Persistent weakness	0	0	0
Hemorrhage	0	0	0
ED transfer	5	0	5
ED visit within 48 hours	6	2	4
Vasovagal reaction	27	3	24
Vasovagal reaction-abort	3	0	3
Aborted procedures	13	4	9
Allergic reaction	7	0	7
Dural puncture	4	3	1

Table A2 Immediate adverse events, Mayo: cervical and thoracic

		Cervical		Thoracic	
Adverse Event	Total N = 1,162	ILESI N = 35	TFESI N = 931	ILESI N = 75	TFESI N = 121
Persistent weakness	0	0	0	0	0
Hemorrhage	0	0	0	0	0
ED transfer	1	0	1	0	0
ED visit within 48 hours	0	0	0	0	0
Vasovagal reaction	8	0	7	1	0
Vasovagal reaction-abort	2	0	2	0	0
Aborted procedures	9	1	8	0	0
Allergic reaction	0	0	0	0	0
Dural puncture	0	0	0	0	0

Table A3 Immediate adverse events, RIC: lumbosacral

Adverse Event	Total N = 4,353	ILESI N = 120	TFESI N = 4,233
Persistent weakness	0	0	0
Hemorrhage	0	0	0
ED transfer	0	0	0
ED visit within 48 hours	3	0	3
Vasovagal reaction	153	0	153
Vasovagal reaction-abort	31	0	31
Aborted procedures	89	1	88
Allergic reaction	1	0	1
Dural puncture	6	1	5

Table A4 Immediate adverse events, RIC: cervical and thoracic

		Cervical		Thoracic	
Adverse Event	Total N = 434	ILESI N = 154	TFESI N = 250	ILESI N = 6	TFESI N = 24
Persistent weakness	0	0	0	0	0
Hemorrhage	0	0	0	0	0
ED transfer	0	0	0	0	0
ED visit within 48 hours	0	0	0	0	0
Vasovagal reaction	7	4	1	0	2
Vasovagal reaction-abort	0	0	0	0	0
Aborted procedures	8	0	7	1	0
Allergic reaction	0	0	0	0	0
Dural puncture	0	0	0	0	0

Table A5 Immediate adverse events, Penn

Adverse Event	Lumbosacral TFESI (N = 404)	Cervical TFESI (N = 80)	Thoracic TFESI (N = 2)
Persistent weakness	0	0	0
Hemorrhage	0	0	0
ED transfer	0	0	0
ED visit within 48 hours	0	0	0
Vasovagal reaction	12	1	0
Vasovagal reaction-abort	0	0	0
Aborted procedures	6	2	0
Allergic reaction	0	0	0
Dural puncture	0	0	0

Table A6 Delayed adverse events, Mayo

	Lumbosacral		Cervical		Thoracic	
Adverse Event	ILESI N = 1,292	TFESI N = 8,911	ILESI N = 35	TFESI N = 931	ILESI N = 75	TFESI N = 121
Neurologic deficit	0	0	0	0	0	0
Hemorrhage	0	0	0	0	0	0
Infection	0	0	0	0	0	0
Increased pain	23	196	0	13	3	2
Complication identified	0	0	0	0	0	0
Central steroid effect	36	177	0	11	0	0
Allergic reaction	1	8	0	2	0	0
CSF leak/spinal headache	1	2	0	0	0	0
Diabetic complication	1	0	0	0	0	0

Table A7 Delayed adverse events, RIC

	Lumbosacral		Cervical		Thoracic	
Adverse Event	ILESI N = 120	TFESI N = 4,233	ILESI N = 154	TFESI N = 250	ILESI N = 6	TFESI N = 24
Neurologic deficit	0	0	0	0	0	0
Hemorrhage	0	0	0	0	0	0
Infection	0	0	0	0	0	0
Increased pain	0	95	4	7	0	1
Complication identified	—	0	0	0	0	0
Central steroid effect	0	186	7	9	0	0
Allergic reaction	0	0	0	0	0	0
CSF leak/spinal headache	0	3	0	0	0	0
Diabetic complication	0	10	0	0	0	0

Table A8 Delayed complications, Penn, by segment type

Adverse Event	Lumbosacral TFESI N = 404	Cervical TFESI N = 80	Thoracic TFESI N = 2
Neurologic deficit	0	0	0
Hemorrhage	0	0	0
Infection	0	0	0
Increased pain	10	3	0
Complication identified	0	0	0
Central steroid effect	1	1	0
Allergic reaction	1	0	0
CSF leak/spinal headache	0	0	0
Diabetic complication	0	0	0