

## Review Article

# Major risks and complications of cervical epidural steroid injections: An updated review

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## Abstract

**Background:** Too many patients, with or without significant cervical disease, unnecessarily undergo cervical epidural steroid injections (CESIs). These include interlaminar (ICESI) and transforaminal ESI (TF-CESI) injections that are not Food and Drug Administration (FDA) approved, have no documented long-term efficacy, and carry severe risks and complications.

**Methods:** Here we reviewed recent reports of morbidity and mortality attributed to the various types of CESIS. Major complications included; epidural hematomas, infection (abscess/meningitis), increased neurological deficits due to intramedullary (quadriplegia/quadriparesis), and intravascular injections (e.g., vertebral artery injections leading to cord, brain stem, and cerebellar strokes). The latter injections leading to strokes were typically attributed to the particulate steroid matter (e.g., within the methylprednisolone injection solution) that embolized into the distal arterial branches.

**Results:** Complications of cervical CESI/TF-CESI injections producing epidural hematoma, new neurological deficits (intramedullary injections), or intravascular injections resulting in strokes to the cord, brain stem, and cerebellum are often underreported. Interestingly, several other cases involving adverse events of CESI/TF-CESI may now be found in the medicolegal literature.

**Conclusions:** Cervical epidural injections (e.g., CESI, ICESI, and TF-CESI) which are not FDA approved, provide no long-term benefit, and are being performed for minimal to no indications. They contribute to significant morbidity and mortality, including; epidural hematomas, infection, inadvertent intramedullary cord injections or cord, brain stem, and cerebellar strokes. Furthermore, these injections are increasingly required by insurance carriers prior to granting permission for definitive surgery, thus significantly delaying in some cases necessary operative intervention, while also subjecting patients at the hands of the insurance companies, to the additional hazards of these procedures.

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**Key words:** Cervical, coma, death, epidural steroid injections, infection, intramedullary, intravascular, paralysis, quadriplegia

## INTRODUCTION

Many patients with even minor cervical complaints without significant magnetic resonance/computed tomography (MR/CT) documentation of significant cervical pathology are increasingly being subjected to high-risk cervical epidural steroid injections (CESIs) [e.g., interlaminar (ICESI) and transforaminal (TF-CESI)]. Major complications of these injections include; epidural hematoma, infection (abscess, meningitis), new neurological deficits (e.g., monoparesis to quadriplegia) due to intramedullary injections, and strokes to the spinal cord, brain stem, and/or cerebellum attributed to intravascular injections among others. Further, these cervical injections are still not approved by the Food and Drug Administration (FDA), and have not been proven to be either safe or effective in the cervical or lumbar spine.

## LACK OF FDA APPROVAL OF CERVICAL EPIDURAL INJECTIONS WITHOUT DOCUMENTATION OF SAFETY/EFFICACY

Here we reviewed the literature between 2004–2013 and 2017–2018 regarding the severe risks/complications/mortality of CESIs, interlaminar (ICESI), and TF-CESI along with selective lumbar ESI (LESI) and TF-LESI. Further, cervical and lumbar epidural injections are still not approved by FDA as their safety/efficacy have never been established. In 2007, Abbasi *et al.* recommended performing prospective blinded randomized controlled trials (RCTs) to document such safety/efficacy; to date, none have yet been adequately completed [Table 1].<sup>[1]</sup> Further, the severe additionally, the severe complications of these procedures are typically under- or unreported in the spinal literature, and are more likely to be found in medicolegal suits [Table 2].

## SUMMARY OF RISKS/COMPLICATIONS OF CERVICAL AND LUMBAR EPIDURAL INJECTIONS 2004-2013

Multiple risk and complications of CESI (ICESI, TF-CESI) were reported between 2004 and 2013. In 2004, Tiso *et al.* quoted the major morbidity/mortality of TF-CESI that included; paresthesias, hematoma, epidural abscess, meningitis, arachnoiditis, subdural/subarachnoid injections, and intraarterial injections resulting in stroke [Table 1].<sup>[12]</sup> Abbasi *et al.* (2007)<sup>[1]</sup> documented an overall 0–16.8% frequency of complications from ICESI [Table 1]. In 2013, Epstein further summarized the morbidity/mortality of cervical injections performed

by various pain management specialists (e.g. radiologists, physiatrists, or anesthesiologists [Table 1]).<sup>[2]</sup> Noteworthy, was the lack of training for all three specialists in how to perform a neurological examination, and for the latter two, how to interpret neuroradiological studies (e.g. MR/CT). Notably, cervical epidural injections were still not FDA approved, and still there are no RCT studies documenting their safety/efficacy. Further, in 2013, the Center for Disease Control (CDC) reported that contaminated steroids resulted in 25 deaths (many due to Aspergillosis), with an added 337 patients sickened, and a total of 14,000 exposed. Other life-threatening complications included spinal fluid leaks (0.4–6%), positional headaches (28%), adhesive arachnoiditis (6–16%), intravascular injections/stroke (7.9–11.6%), hydrocephalus, air embolism, urinary retention, allergic reactions, blindness, neurological deficits/paralysis, hematomas, seizures, and death.

## SUMMARY OF RISKS/COMPLICATIONS OF CERVICAL AND LUMBAR EPIDURAL INJECTIONS 2017-2018

In 2017, Epstein (2017) again focused on the continued risks/complications of both cervical (CESI, ICESI, TF-CESI) and lumbar (LESI, ILESI, TF-LESI) ESI [Table 2].<sup>[3]</sup> It was noted that about 9 million epidural injections are performed per year in the US, and they are still not FDA approved. In five of the six cervical ESI studies that Epstein identified, inadvertent dural punctures (CESI) resulted in intramedullary spinal cord injuries and paralysis, or intravascular vertebral artery injections resulted in strokes (e.g., to the spinal cord/brain stem/cerebellum). Schneider *et al.* (2018) additionally discussed how CESI contributed not only to intramedullary and intravascular injections, leading to embolic infarcts (e.g., from particulate steroids), but also to hematomas, abscesses, vertebral artery dissections, pain, side effects of steroids, and vasovagal reactions [Table 2].<sup>[10]</sup>

## RISKS OF INTRAMEDULLARY EPIDURAL SPINAL INJECTIONS

Cervical ESIs and rarely high LESIs (e.g., CESI, ICESI, TF-CESI, TF-LESI) may result in inadvertent intramedullary cervical and thoracic/conus cord injections [Tables 1 and 2].<sup>[5,7]</sup> Landers (2017) presented a patient who, immediately following an ICESI, became quadriplegic due to an intramedullary injection [Table 2].<sup>[5]</sup> The authors presented other cases of CESI resulting in intramedullary injections, and recommended that practice guidelines be revised to avoid such injuries in the future.

**Table 1: Summary of articles on CESIs 2004-2013**

Author [ref] Year	#Cervical ESI	Procedures performed	Complications	Complications	Complications
Huntoon <sup>[4]</sup> 2004	64 yo M Lumbar TF-ESI attempted Failed	Left L1 TF-ESI 1 mL iopamidol with 5 mL 0.125% bupivacaine and 40 mg triamcinolone	Within 3 minutes irreversible paraplegia	MR high-cord signal T11-12 Cord stroke High-dose steroids	Remained plegic Complications TF-ESI Cord stroke Intravascular injections
Tiso <sup>[12]</sup> 2004	TF-CESI Right C5-6 Cervical Massive Cerebellar Infarct	Complications TF-CESI Paresthesias Hematoma Abscess Meningitis Arachnoiditis	Subdural Paralysis Stroke from intraarterial injection Steroid particles	Performed with biplanar fluoroscopy test injection contrast	Quadriplegia immediate/total Despite decompression no improvement
Ludwig <sup>[7]</sup> 2005	Cervical cord stroke TF-CESI	53 yo M Left C6 TF-CESI/Fluoro In 10-15 Minutes: Paralysis LUE and both LE	1 <sup>st</sup> MR: Negative	2 <sup>nd</sup> MR 24 hours. High T2 cord signal C0-C4/C5/Stroke	Cord infarct/stroke Incomplete quadriplegia Unchanged
Epstein <sup>[2]</sup> 2013	AE all cervical and lumbar CESI, TF-CESI, LESI, TF-LESI	Pain management: Radiologists, physiatrists anesthesiologists Not FDA approved	Risks: 6% CSF leak 28% Headache Death Infection Abscess Paralysis	Risks: 16% Arachnoiditis 11.6% Stroke Blindness Hematomas Seizures	Center for Disease Control 25 deaths Aspergillosis 337 Sickened 14,000 Exposed to contaminated steroids
Abbasi <sup>[11]</sup> 2007	Complication Interlaminar CESI (ICESI)	Review Major AE	4 Major cerebellar and brain stem strokes	Risks TF-CESI with methylprednisolone	Complication rate 0-16.8%
Scanlon <sup>[9]</sup> 2007	TF-CESI 8 Brain and spinal cord Strokes ETIOLOGY: Cervical Radicular Complaints No RCT-documented efficacy	Survey American Pain Society 21.4% Responses (287/1340) 78 AE: 16 Vertebrobasilar brain strokes 112 Cervical cord strokes 2 Both brain/cord strokes/ infarcts	Significant risks AE and neurological injury with TF-CESI 78 AE: 13 cases FATAL	Fatalities: 5 Brain stroke 1 Brain/spinal strokes 1 High spinal anesthesia 1 Seizure 5 Undefined	All 4 cases with methylprednisolone; 3 cerebellar strokes 1 Posterior cerebral stroke (3 Fatal) Stroke due to: Embolism particulate steroids

ESI: Epidural spinal injections, CESI: Cervical epidural steroid injections, MI: Myocardial infarction, CTFESI: Cervical transforaminal epidural steroid injections, CILESI: Cervical interlaminar epidural steroid injection, CEA: Cervical epidural abscess, LUE: Left upper extremity, LE: Lower extremities, FDA: Food and Drug Administration, RCT: Randomized controlled trials, AE: Adverse events

## CERVICAL INTRAVASCULAR EPIDURAL INJECTIONS

Several articles identified intravascular CESI resulting in major morbidity/mortality [Table 1].<sup>[1,7,9,12]</sup> In 2004, Tiso *et al.* presented a patient with a C5-C6 disc herniation on MR; following a C5-C6 TF-CESI, he developed a massive cord/brain stem/cerebellar infarct attributed to an intraarterial injection with resultant embolization of particulate steroids [Table 1].<sup>[12]</sup> This occurred even after confirming accurate needle placement with biplanar fluoroscopy, after performing several heme-negative aspirations, and utilizing trial injections of contrast. Despite emergent cerebellar decompression, the patient never recovered. In 2005, Ludwig and Burns observed a 53-year-old male who developed left upper and bilateral lower extremity quadriplegia 15 min following a left C6 TF-CESI performed under fluoroscopy [Table 1].<sup>[7]</sup> Although the first MR showed no intramedullary cord signal

changes, the second MR 24 h later revealed a C0-C4/5 intramedullary cord stroke (e.g., patchy high signal intensity in the cord) attributed to an intravascular injection (e.g., embolization of particulate steroids; this resulting in permanent paralysis). Abbasi *et al.* (2007)<sup>[11]</sup> added an additional four cases of major cerebellar/brain stem strokes [Table 1]. Scanlon *et al.* (2007) further questioned, after looking at the incidence of stroke following TF-CESI, whether these procedures were “more dangerous than we think” [Table 1]?<sup>[9]</sup> They again confirmed the lack of adequate RCTs to establish the safety/efficacy of TF-CESI. Additionally, the reviewed eight cases of brain/spinal cord infarction appearing in the literature, and added four cases of major cerebellum/brainstem infarction. Interestingly, when they surveyed US physician members of the American Pain Society [e.g., 21.4% response rate (287 of 1340)], they identified 78 complications of TF-CESI. These included; 16 vertebrobasilar brain infarcts, 12 cervical spinal cord infarcts, and 2 combined brain/

**Table 2: Summary of articles on CESIs 2017-2018**

Author [ref] Year	#Cervical ESI	Procedures performed	Complications	Complications	Complications
Landers <sup>[5]</sup> 2017	Spinal cord injury	Attempted cervical interlaminar ESI	Practice guidelines to avoid these complications		
Zhang <sup>[13]</sup> 2017	Cervical ESI Punctured twice Neck pain Elevated WBC CEA	MR confirmed C6-T8 case Review Treatment: IV vancomycin >4 weeks and imipenem and cilastatin	Rare complication Large lesions require surgery	2 Weeks after IV therapy: MR improved <WBC and <CRP and <neck/back pain	Rapid diagnosis and treatment emphasized No recurrence 3 months later
Smith <sup>[11]</sup> 2017	14,247 Admission over 8 years 1182 CESI 4617 LESI	Lumbar Interlaminar injections 13 required neurosurgery	0.51% CESI 0.15% LESI 0.09% all neurosurgical admissions	7 Hemorrhages 3 Infections (LESI related) 3 Dural penetrations	Anticoagulation increased risk Hematoma Surgery: good results
Epstein <sup>[3]</sup> 2017	AE LESI Headaches Intracranial hypotension	AE LESI SDH 6 cranial palsies Hematomas	AE CESI IM injections Strokes, clots, cord/brain stem/vertebral	CESI 5 of 6 studies; dural punctures with CESI	CESI Intramedullary cord injury, stroke to vertebral
Lee <sup>[6]</sup> 2017	Cervical roots susceptible to injury: selective root blocks	74 patients Cervical radiculopathy Prior to injection	US-guided nerve block 2012-2014 Evaluated vessels around C5, C6, C7	US identify vessels: surround roots prior to injection	Multiple susceptible vessels: At C5, C6, C7 levels C5 (4), C6 (9), C7 (10)
Schneider <sup>[10]</sup> 2018	Complication of CESI CTFESI CILESI	Aberrant needle placement	Stroke Hematoma Abscess Intramedullary injection	CTFESI Embolic Vertebral injection particulate steroids	Most common AE CTFESI or CILESI: Pain Vasovagal Events
Sanders <sup>[8]</sup> 2018	Epidural hematoma 79 yo M	ICESI Did not stop 81 mg ASA Prophylaxis for MI	American Society Regional Anesthesia and Pain Medicine Guidelines	Recommend; Hold ASA 5 days before ICESI medications	Postoperative hematoma

ESI: Epidural spinal injections, CESI: Cervical epidural steroid injections, MI: Myocardial infarction, CTFESI: Cervical transforaminal epidural steroid injections, CILESI: Cervical interlaminar epidural steroid infection, CEA: Cervical epidural abscess, SDH: Subdural hematoma, AE: Adverse events, US: Ultrasound

spinal cord infarcts: 13 of these patients sustained fatal injuries [Table 1]. They observed that TF-CESIs correlated with an unacceptably high incidence of complications that included; intraarterial injections/strokes/embolism (e.g., to the basilar artery, midbrain, pons, cerebellum, thalamus, temporal, and occipital lobes), along with the occasional vertebral artery perforation, dissection, thrombosis, or vasospasm.

### UTILIZING ULTRASOUND TO IDENTIFY VESSELS SURROUNDING C5-C7 CERVICAL NERVE ROOTS PRIOR TO SELECTIVE CERVICAL C5-C7 NERVE ROOT BLOCKS

Lee *et al.* (2017) utilized ultrasound (US) to document the size/location/number of vulnerable and susceptible perineural blood vessels prior to performing selective nerve root blocks from C5 to C7 (2012–2014) [Table 2].<sup>[6]</sup> Many vessels were at or in the projected target pathway for selective nerve root blocks; C5 level ( $n = 4$ ; 5.45%), C6 ( $n = 9$ ; 12.16%), and C7 ( $n = 10$ ; 13.51%). This finding confirmed the increased susceptibility to arterial as well as venous intravascular injections during these procedures (e.g. stroke, hematoma, and others).

### HIGH LUMBAR L1 TRANSFORAMINAL ESI INJECTION/CORD STROKE

In 2004, Huntoon and Matin (2004) identified a 64-year-old male with a history of multiple prior lumbar operations, who underwent a left L1 TF-LESI; it contained 1 mL of iopamidol (Isovue), 5 mL of 0.125% bupivacaine, and 40 mg of triamcinolone [Table 1].<sup>[4]</sup> Within 3 min, he was irreversibly paraplegic. The MRI showed a cord infarct (e.g., hyperintense intramedullary cord signal on T2-weighted images) at the T11/L2 level (e.g., conus medullaris). Despite the utilization of high-dose steroids, the patient's deficit remained fixed.

### INCIDENCE OF HEMORRHAGES DUE TO VARIOUS CERVICAL/LUMBAR EPIDURAL STEROID INJECTIONS

Two studies cited the risks of peri-procedural hematomas in patients undergoing CESI and LESI [Table 2].<sup>[8,11]</sup> Smith *et al.* (2017), over an 8-year period, identified complications following 1182 ICESI and 4617 ILESI [Table 2].<sup>[11]</sup> Thirteen patients required emergency neurosurgery to address; 7

hemorrhages, 3 infections (all after lumbar injections), and 3 inadvertent dural punctures. Notably, six of seven patients developed epidural hematomas despite being managed with current guidelines [e.g., requiring prolonged cessation of anticoagulation ( $n = 3$ ), or taking only aspirin ( $n = 3$ )]. Surgical decompression in all cases fortunately resulted in neurological improvement. In the case study from Sanders *et al.* (2018), a 79-year-old male continued prophylactic baby aspirin therapy (81 mg) prior to a LESI due to a recent myocardial infarction [Table 2].<sup>[8]</sup> The patient and his physicians failed to follow the antiplatelet and anticoagulation guidelines of the American Society of Regional Anesthesia and Pain Medicine that required the 81 mg of ASA be held for 5 days before such a procedure. The result was an immediate postinjection epidural hematoma and permanent paraparesis.

## CERVICAL EPIDURAL ABSCESS DUE TO CESI

Zhang *et al.* (2017) noted that CESI rarely result in cervical epidural abscess (CEA).<sup>[13]</sup> In some cases they may be effectively treated with antibiotic therapy alone, but in others, they may warrant operative debridement [Table 2].<sup>[13]</sup> Their patient had a CESI, and later developed a C6-T8 CEA on MR. The patient was effectively treated with 4 weeks of intravenous vancomycin, imipenem, and cilastatin. Following just 2 weeks of therapy, the patient's symptoms and laboratory studies improved [e.g., for the latter, the white blood cell count decreased along with the neutrophil count, and C-reactive protein (CRP)]. Three months later, the patient fully recovered, and the follow-up MR documented complete resolution of the abscess. Notably, in the US, infectious disease consultants would typically require a minimum of 6 weeks of intravenous antibiotic therapy, followed in some cases by long-term suppressive oral antibiotics.

## CONCLUSION

Cervical ESI (CESI, ICESI, TF-CESI) and lumbar ESI (LESI, ILESI, TF-LESI) are not FDA-approved and

have no RCT-documented long-term safety or efficacy. Further, CESI and occasionally high LESI (e.g., TF-LESI at the L1 level) risks include severe morbidity and mortality. Intramedullary or intravascular injections result in irreversible paralysis and/or strokes (e.g., cord, brain stem, and cerebellar strokes).

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## Conflicts of interest

There are no conflicts of interest.

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