



## ■ SYSTEMATIC REVIEW

# Cervical transforaminal epidural steroid injections for radicular pain

A SYSTEMATIC REVIEW

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### Aims

Cervical radiculopathy is a significant cause of pain and morbidity. For patients with severe and poorly controlled symptoms who may not be candidates for surgical management, treatment with transforaminal epidural steroid injections (CTFESI) has gained widespread acceptance. However, a paucity of high-quality evidence supporting their use balanced against perceived high risks of the procedure potentially undermines the confidence of clinicians who use the technique. We undertook a systematic review of the available literature regarding CTFESI to assess the clinical efficacy and complication rates of the procedure.

### Methods

OVID, MEDLINE, and Embase database searches were performed independently by two authors who subsequently completed title, abstract, and full-text screening for inclusion against set criteria. Clinical outcomes and complication data were extracted, and a narrative synthesis presented.

### Results

Six studies (three randomized controlled trials and three non-randomized observational studies; 443 patients) were included in the final review. The aggregate data support the efficacy of CTFESI in excess of the likely minimal clinically important difference. No major complications were described.

### Conclusion

There is increasing evidence supporting the efficacy of CTFESI. Concerns regarding the occurrence of catastrophic complications, widely shared in the case report and anecdotal literature, were not found when reviewing the best available evidence. However, the strength of these findings remains limited by the lack of highly powered high-level studies and the heterogeneity of the studies available. Further high-quality studies are recommended to address the issues of efficacy and safety with CTFESI.

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### Introduction

Cervical radiculopathy is a recognized source of significant pain and morbidity. Its prevalence is 1.2 to 5.8 per 1,000 population,<sup>1</sup> with peak incidence in the fourth and fifth decades.<sup>2</sup> The lower cervical roots (C6-C8) are most frequently implicated.<sup>2</sup> The pathophysiology includes mechanical compression of the involved nerve root(s) caused by intervertebral disc herniation, impingement from osteophytes or foraminal stenosis, and a concurrent pro-inflammatory cascade.<sup>2</sup>

The natural history of cervical radiculopathy is variable. When caused by a disc herniation, one systematic review has suggested substantial improvement often occurs in four to six months, with resolution in two to three years.<sup>3</sup> Even when the underlying pathology is foraminal narrowing secondary to bony encroachment, resolution can be expected in many patients, although the rate of resolution is lower than following acute disc prolapse.<sup>4</sup> For those with intractable symptoms who fail nonoperative management, surgical options include anterior cervical discectomy and

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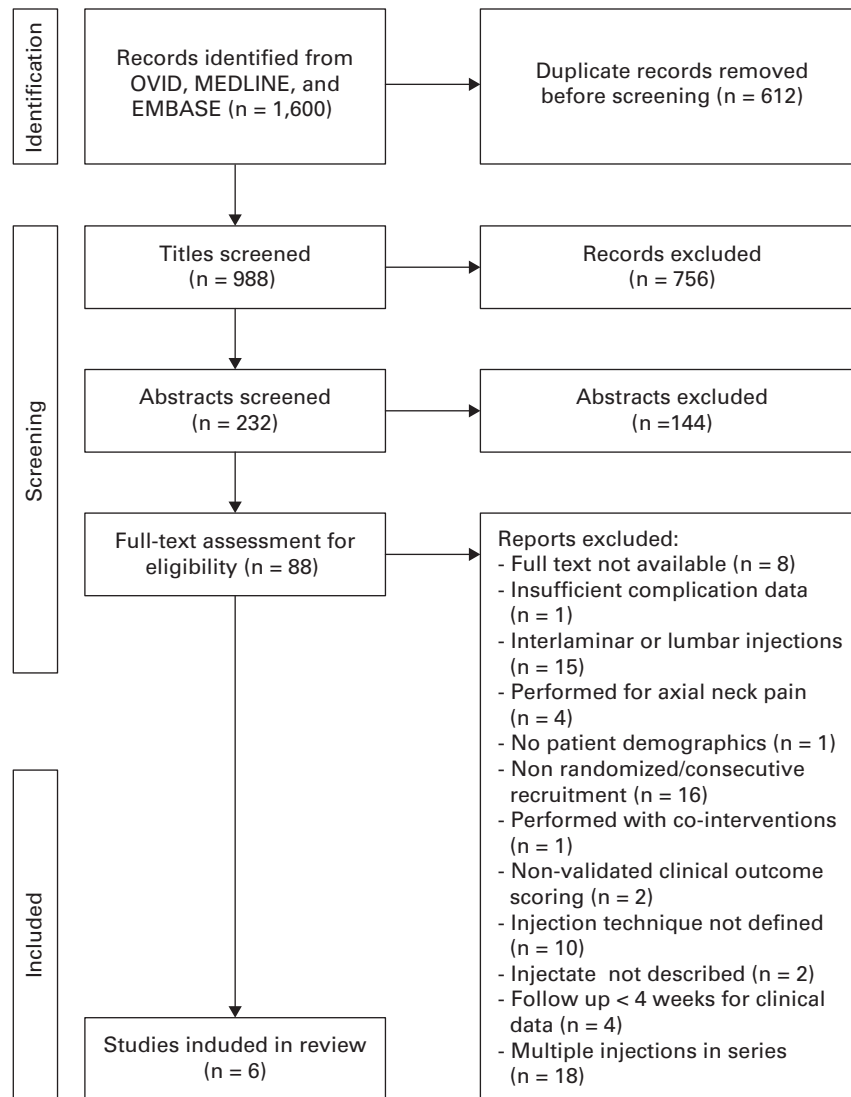


Fig. 1

Preferred Reporting Items for Systematic Reviews and Meta-Analyses<sup>17</sup> flowchart demonstrating article exclusions at each phase of the systematic review.

fusion (ACDF), disc arthroplasty, and posterior decompressive procedures. Of these, the most frequently performed procedure is ACDF,<sup>5</sup> although there is no strong evidence suggesting superiority of one approach over another.<sup>6</sup>

For people with intrusive and incompletely controlled nerve root pain who are not candidates for surgery, epidural steroid injections are commonly used. Epidural steroid is thought to reduce root inflammation and inhibit the propagation of the pro-inflammatory cascade and pain-mediating peptides,<sup>2</sup> as well as stabilizing neural membranes and modulating conduction, hence its reported efficacy in non-inflammatory conditions.<sup>7</sup> As many disease processes such as disc herniation are likely to resolve spontaneously given time, nerve root blocks are an important treatment option for symptomatic relief while awaiting natural resolution. Without this intervention, there can be an extensive interval between conservative and surgical options. Additionally, level-specific blocks can have an important diagnostic role

if the presence of multiple levels of degenerative change causes uncertainty regarding the specific nerve root(s) provoking pain.<sup>8,9</sup> However, epidural steroid injections have been criticized as lacking an evidence base, and have been associated with a number of major complications.<sup>10</sup>

Previous studies identified a lack of high-quality evidence to either support or discourage cervical epidurals, with significant heterogeneity of available data. ‘Cervical epidural steroid injection’ may refer to both non-selective interlaminar or targeted transforaminal injections, usually with, but sometimes without, image guidance. Multiple indications for the injections have been applied (e.g. axial neck pain, radiculopathy), caused by a range of pathological or degenerative processes which may coexist. A variety of injectables have been used, and treatment goals also vary, with some injections performed for symptomatic relief and others for diagnostic purposes.<sup>7</sup>

**Table 1.** Summary of quality assessment of included studies. Final decision regarding inclusion was made by consensus after appraisal.

Variable	Obernauer et al <sup>18</sup>	Bureau et al <sup>19</sup>	Dreyfuss et al <sup>20</sup>	Bise et al <sup>21</sup>	Wald et al <sup>22</sup>	Kumar and Gowda <sup>23</sup>
Study type	RCT	RCT	RCT	Cohort	Cohort	Cohort
1. Was the study question or objective clearly stated?	Y	Y	Y	Y	Y	Y
2. Were eligibility/selection criteria for the study population prespecified and clearly described?	Y	Y	Y	Y	Y	Y
3. Were the participants in the study representative of those who would be eligible for the test/service/intervention in the general or clinical population of interest?	Y	Y	Y	Y	Y	Y
4. Were all eligible participants that met the prespecified entry criteria enrolled?	Y	N	Y	Y	Y	Y
5. Was the sample size sufficiently large to provide confidence in the findings?	N	N	N	Y	Y	N
6. Was the test/service/intervention clearly described and delivered consistently across the study population?	Y	Y	Y	Y	Y	Y
7. Were the outcome measures prespecified, clearly defined, valid, reliable, and assessed consistently across all study participants?	Y	Y	Y	Y	Y	Y
8. Were the people assessing the outcomes blinded to the participants' exposures/interventions?	Y	N	N	N/A	N/A	N
9. Was the loss to follow-up after baseline 20% or less? Were those lost to follow-up accounted for in the analysis?	Y	Y	Y	N	N	Y
10. Did the statistical analysis examine changes in outcome measures from before to after the intervention? Were statistical tests done that provided p-values for the pre-to-post changes?	Y	N	Y	Y	Y	N
11. Were outcome measures of interest taken multiple times before the intervention and multiple times after the intervention (i.e. did they use an interrupted time-series design)?	N	Y	N	Y	Y	Y
12. If the intervention was conducted at a group level (e.g. a whole hospital, a community) did the statistical analysis take into account the use of individual-level data to determine effects at the group level?	N/A	N/A	N/A	N/A	N/A	N/A
Reviewer 1	Fair	Fair	Good-Fair	Good-Fair	Good	Good-Fair
Reviewer 2	Fair	Good	Good	Good	Good	Fair

N/A, not applicable; RCT, randomized controlled trial.

The transforaminal epidural approach is considered more appropriate than the non-selective interlaminar approach to precisely target an injection to the relevant anatomical site and achieve an optimal therapeutic effect. However, there is as yet limited evidence supporting its superiority.<sup>7</sup> Early reports reviewing the efficacy of all routes of epidural administration, at both lumbar and cervical levels, found moderate evidence for transforaminal injections for the treatment of radiculopathy.<sup>11,12</sup> However, subsequent systematic reviews in 2013<sup>13</sup> and 2018,<sup>14</sup> specifically relating to fluoroscopically guided transforaminal injection in the cervical spine, found only low-grade evidence in favour.

To try to improve understanding, we carried out an updated systematic review of the available randomized and non-randomized literature relating to cervical transforaminal epidural steroid injections (CTFESI). Since many centres use imaging methods other than fluoroscopy, we included CT and ultrasound (USS) to better reflect current practice. The primary aim of this systematic review was to review the clinical efficacy of CTFESI. Secondary objectives included a review of complications, both immediate and delayed, and the ability to avoid surgery.

## Methods

**Eligibility criteria.** Ethical approval was not required for this study. Studies involving cervical epidural steroid injections

were reviewed. Inclusion criteria were randomized trials or consecutive non-randomized series reporting results of transforaminal injections performed on adults (aged 18 years or over) for radicular pain. Exclusion criteria included studies reporting on epidural steroid injections for axial neck pain, those reporting on interlaminar injections, or studies published with insufficient procedural details (including composition of injections). Reports describing injections performed without image guidance, studies with cohorts of ten patients or fewer, reports of investigations with less than four weeks' follow-up, and studies reporting data when recipients received two or more injections at the same vertebral level sequentially were also excluded.

**Information sources and search.** Searches of the OVID, MEDLINE, and Embase databases were performed independently by two authors (ZMB, BJO) in March 2021. English-language articles published between 1946 and the present day were considered for inclusion. The following search strategy was used: ((cervical OR neck OR upper ext\* or arm) AND (transforaminal OR nerve root block\* OR nerve block\* OR selective nerve OR epidural\* OR radicul\* OR periradicul\*)) AND (steroid\* OR inject\* or block\*).

**Study selection.** The same two blinded authors subsequently completed title, abstract, and full-text screening for inclusion, with cross-verification and resolution of disagreement

**Table II.** Summary of outcomes extracted from included studies. Where possible, percentages and absolute values of change have been provided for consistency of reporting across studies and pain scores reported on a ten-point scale.

Study	Design	Intervention	Participants (n; baseline)	Participants (n; follow-up)	Outcomes	Complications
Obernauer et al <sup>18</sup>	RCT comparing CT with USS-guided transforaminal injections	CT or USS-guided CTFESI with betamethasone (particulate)	40 (20 each arm)	40 (100%) at 4 weeks	Mean reduction of 59.5% in VAS scores (absolute value 3.75)	2 minor complications
Bureau et al <sup>19</sup>	Double blind RCT comparing transforaminal with transfacet injections	CT-guided CTFESI with dexamethasone and lidocaine (non-particulate)	27	27 (100%) at 4 weeks	Mean reduction of 17.8% in VAS and 12.8% in NDI (as treated analysis)	None
Dreyfuss et al <sup>20</sup>	Unblinded RCT comparing particulate and non-particulate steroid	XR-guided CTFESI with triamcinolone (particulate) or dexamethasone (non-particulate)	30 (15 each arm)	30 (100%) at 4 weeks	Mean reduction of 52.6%. 63.5% had improvement in VAS > 50% at four weeks (absolute value of improvement 2.6)	None
Bise et al <sup>21</sup>	Prospective cohort study comparing CTFESI (anterior and posterior techniques) and transfacet CT-guided injections	CT-guided CTFESI with cortivazol+ lidocaine (particulate)	66	61 (92%) at 6 weeks 42 (64%) at 6 months	Median reduction of 27% and 25% (absolute values 4 and 5) in VAS scores at six weeks and 33% and 50% (absolute values 4 and 3) at six months. Reduction of NDI of 18% and 20% (absolute values of 30 and 30) at 6 weeks and 10% and 20% (absolute values 30 and 22) at 6 months (between transforaminal techniques).	None
Wald et al <sup>22</sup>	Retrospective cohort study	CT-guided CTFESI with dexamethasone using either an anterolateral or posterior approach (non-particulate)	247	120 (49%) at 2 months	40% had a reduction > 50% in VAS score at 2 months. Absolute value 2.1.	4 minor complications
Kumar and Gowda <sup>23</sup>	Retrospective cohort study	XR-guided CTFESI with triamcinolone (particulate)	33	30 (91%) at 6 weeks 28 (85%) at 1 year	Mean reduction in cohort VAS score of 70% at 6 weeks and 73 at one year (absolute values 5.2 and 5.4). Reduction in NDI of 52.6% at 6 weeks and 53.5% at one year (absolute values 35.2 and 35.8).	None

CTFESI, cervical transforaminal epidural steroid injections; NDI, Neck Disability Index; RCT, randomized controlled trial; USS, ultrasound; VAS, visual analogue scale; XR, x-ray.

by consensus at each stage. Standardized proformas were used by reviewers at the abstract and full-text screening stages (Supplementary Material).

**Risk of bias in individual studies.** Prior to a final decision regarding inclusion, articles underwent risk-of-bias appraisal using the study quality assessment tools supplied by the Heart, Lung, and Blood Institute of the USA National Institutes of Health.<sup>15</sup>

**Data extraction.** Bibliographic information was recorded for each study, as well as the inclusion and exclusion criteria, participant demographic details, diagnosis, mode of image guidance, and injectate composition. Data extracted to satisfy the primary outcome were the reduction of pain or disability recorded using a validated scoring system, such as a visual analogue scale (VAS) or Neck Disability Index (NDI).<sup>16</sup> The minimum duration of follow-up was set at four weeks, but where studies provided serial measurements, all the results were extracted and analyzed. Information relating to the secondary outcome measures of clinical complication rates (e.g. cerebrovascular event) or radiological complications (e.g. inadvertent vascular injection) and avoidance of surgery were also extracted.

Difficulties in formal statistical meta-analysis were anticipated because of the expected heterogeneity of studies described in previous reviews. Therefore, it was determined a priori that should the data support rigorous random-effect model meta-analysis then this would be presented, but if that was not possible, a narrative synthesis would be presented instead. Where formal meta-analysis is not feasible, efforts have been made to present standardized mean differences (SMDs) using the standard deviation of the differences as a denominator, either as reported or statistically derived from the reported data, to inform the effect size of the intervention and aid ease of interpretation across studies.

## Results

The results of the search strategy and subsequent study selection are provided as a Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)<sup>17</sup> flowchart in Figure 1. After eliminating duplicates, 988 titles were screened, yielding 232 abstracts, and subsequently 88 full-text manuscripts were reviewed for inclusion. Six studies were included in the final review, consisting of three randomized controlled trials

**Table III.** Standardized mean difference as a measure of effect size concerning relief of radicular pain due to cervical transforaminal epidural steroid injections.

Study	Follow-up timeframe	Included sample size	Post-intervention improvement (SD)	Standardized effect size
Obernauer et al <sup>18</sup>	4 weeks	40	59.5% (40.8%)	1.5
Bureau et al <sup>19</sup>	4 weeks	27	17.8% (45) (VAS) 12.8% (32.2) (NDI)	0.4
Dreyfuss et al <sup>20</sup>	4 weeks	30	2.6 (incalculable) (VAS)	Incalculable from the presented data
Bise et al <sup>21</sup>	Incalculable from the presented data (non-parametricity)			
Wald et al <sup>22</sup>	2 months	120	2.1 (2.8) (VAS)	0.75
Kumar and Gowda <sup>*23</sup>	6 weeks	30	5.1 (1.7) (VAS) 35.2 (12.9) (NDI)	2.7 to 3

Standard deviation of the difference used as denominator.

\*Standard deviations were combined across groups.

†Estimation of standard deviation from 95% confidence intervals.

NDI, Neck Disability Index; SD, standard deviation; VAS, visual analogue scale.

(RCTs)<sup>18–20</sup> and three non-randomized observational studies comprising 443 CTFESIs.<sup>21–23</sup> Quality appraisal of the included studies is summarized in Table I. Regarding randomization protocols of the RCTs, simple randomization by random-number table was used in one,<sup>18</sup> block randomization in one,<sup>19</sup> and an unspecified method in one.<sup>20</sup>

Formal statistical meta-analysis was not possible due to variation in, or lack of, control groups, inconsistent follow-up periods, and heterogenous reporting of outcomes. The characteristics of the included studies are summarized in Table II.

**Short-term radicular pain relief (four to eight weeks).** All six studies reported short-term clinical outcome data, but these were incomplete, referring to only 308 of the 443 enrolled patients (70%). Three studies were RCTs comparing imaging modality, injection technique, and injected material, respectively.<sup>18–20</sup> No studies directly compared CTFESI with other treatment options or placebo. The remainder of the included studies were either prospective<sup>21</sup> or retrospective<sup>22,23</sup> cohort studies. VAS or NDI were the reported outcome measures. One study by Wald et al<sup>22</sup> also used the Roland Morris Disability Index,<sup>22,24</sup> but as this outcome measure has not been validated in the cervical spine, these data were excluded from review.

Results were variably reported using either a percentage change, the proportion of patients achieving a 50% reduction in pain score, or by presentation of the absolute values, making direct comparison across studies difficult. Where possible, to aid in consistency of reporting and ease of interpretation across studies, we have presented the reported data as percentage improvement and improvement in absolute values on a ten-point scale.

The short-term decrease in pain scores following injection varied greatly both within and between studies. Mean reduction in pain scores ranged from 18%<sup>19</sup> to 70%<sup>23</sup> (Table II). Wald et al<sup>22</sup> and Dreyfuss et al<sup>20</sup> considered a 50% reduction in the pain score to be clinically significant, and reported that between 35% and 63.5% of patients had a significant reduction in pain scores in the short term. It was possible to derive mean or median percentage change in five of the six studies. This was greater than 50% in three,<sup>18,20,23</sup> and less than 50% in two.<sup>19,21</sup> Percentage change could not be calculated from the presented data in one.<sup>22</sup> Bureau et al,<sup>19</sup> Bise et al,<sup>21</sup> and Kumar and Gowda<sup>23</sup>

also reported NDI before and after CTFESI, showing 12.8%, 18%, and 35.2% improvement, respectively.

**Longer-term pain relief (eight weeks to one year).** Wald et al,<sup>22</sup> Bise et al,<sup>21</sup> and Kumar and Gowda<sup>23</sup> reported longer-term clinical outcomes at two months, six months, and one year, respectively. Wald et al<sup>22</sup> found 40% of patients still had greater than 50% improvement two months following injection, although there was a significant (51%) loss to follow-up. Bise et al<sup>21</sup> reported a median VAS reduction of 33% at six months following injection in one of their cohorts, and 50% in the other, with corresponding NDI improvements of 10% and 20%. Kumar and Gowda<sup>23</sup> reported improvements in VAS of 73% and in NDI of 53.5% one year following injection. They reported no statistical difference between scores at six weeks and one year.

**Prognostic indicators.** Bise et al<sup>21</sup> attempted to identify factors that were associated with a favourable outcome following injection, and reported a significant association between laterality and response, but were unable to demonstrate significant association between age, sex, weight, or duration of pain with response. Kumar and Gowda<sup>23</sup> found no association with laterality or sex, but did report that increasing age, and those undergoing CTFESI at the C6 or C7 levels, had a significantly larger reduction in VAS scores at six weeks.

**Effect size of the intervention.** No study directly reported overall effect size of the intervention. In two studies, effect size could not be calculated from the presented data, due to non-parametricity in one<sup>21</sup> and insufficient presented data in the other.<sup>20</sup> The results of our calculation of effect sizes are shown in Table III. SMD of the effect of CTFESI on patient-reported outcomes ranged from 0.4 to 3.

**Complications.** No major complications and only six minor complications were reported across the included studies, equating to an incidence of 1.35%. Obernauer et al<sup>18</sup> reported one transient episode of upper limb numbness and one self-limiting episode of vertigo. Wald et al<sup>22</sup> noted four episodes of vasovagal syncope.

**Avoidance of surgery/eventual treatment outcome.** Two of the six studies provided details of conversion to surgical intervention after CTFESI.<sup>21,23</sup> Kumar and Gowda<sup>23</sup> reported that 6.67% (n = 2) had surgery six weeks after injection and that this conversion rate was maintained at two years. Bise et al<sup>21</sup>



reported that 20% ( $n = 13$ ) patients had surgery at six months, but acknowledged that CTFESI is frequently used as a diagnostic procedure prior to planned surgical intervention in their practice, possibly accounting for the relatively high conversion rate. **Particulate versus non-particulate steroid preparations.** Dreyfuss et al<sup>20</sup> performed a RCT in 30 patients directly comparing particulate and non-particulate steroids (15 per arm). No significant differences in VAS scores at four weeks were found and no complications were reported. No other study directly compared the use of particulate or non-particulate steroids. In total, 154 injections used particulate and 289 non-particulate preparations. Two minor complications (1.3%) were encountered in the particulate group and four (1.4%) in the non-particulate group. This was not statistically significant ( $p > 0.999$ , Fisher's exact test).

**Imaging modality.** Four studies (360 injections; 81.3%) used CT guidance for CTFESI,<sup>18,19,21,22</sup> injections under ultrasound control were reported in one study (20 injections; 4.5%),<sup>18</sup> and two studies used fluoroscopy (66 injections; 14.9%).<sup>20-23</sup> A single study by Obernauer et al<sup>18</sup> directly compared USS- and CT-guided CTFESI. No significant differences in clinical outcomes were demonstrated.

## Discussion

Recent systematic reviews relating to the efficacy of CTFESI have shown evidence in favour of their use, but they recognized the overall quality of evidence was low and tempered by concern regarding significant risks.<sup>13,14</sup> Our review of the best available current evidence continues to support the contention that CTFESI may be associated with significant symptomatic relief.

Considering minimal clinically important difference (MCID) in outcomes as a measure of efficacy, we are not aware of any studies reporting MCID following CTFESI. However, the MCID has been reported for VAS and NDI scores following surgery for radiculopathy.<sup>25,26</sup> Given the very different risk profiles of surgery versus CTFESI, the MCID for CTFESI is likely to be less than the MCID for surgery, but for the purposes of the following discussion, the values for the latter have been taken as a proxy. Alternatively, clinically meaningful change, which is represented by 30% improvement rather than a discrete value, can also demonstrate efficacy.<sup>27</sup>

Considering VAS scores, MCID values of between 3.0<sup>26</sup> and 4.1<sup>25</sup> points have been suggested. Of the studies reporting discrete VAS scores, two report short-term outcomes greater than the upper estimate of the MCID,<sup>21,23</sup> one reports improvements that lie within the range of estimates,<sup>18</sup> and two report improvements less than the reported MCID for fusion surgery.<sup>20,22</sup> In the longer term, one study continued to demonstrate benefit in excess of these estimates,<sup>23</sup> and one showed benefit lying between the upper and lower bound.<sup>21</sup> Most studies included in the review therefore support an effect beyond the MCID for surgery, and all beyond the likely MCID for CTFESI.

Four studies provided a figure of percentage improvement, and these data were derived in one further study, allowing an assessment of clinically meaningful improvement. At their final follow-up, four studies demonstrated a successful outcome

using this metric,<sup>18,20,21,23</sup> whereas one did not.<sup>19</sup> Therefore, a majority of studies support a clinically meaningful improvement following CTFESI.

MCID values for the NDI vary widely, ranging from 7.5%<sup>26</sup> to 17.3%.<sup>25</sup> Two of three studies which reported NDI scores showed outcomes in excess of the upper margin at both short and longer terms,<sup>21,23</sup> supporting the efficacy of CTFESI, while the third reported a mean NDI reduction of 12.8%,<sup>19</sup> which lies between the two given MCID values.

Due to the variable methods used to report results in the included studies, SMDs were selected as an estimate of effect size. However, the small sample size in some of the included studies could lead the SMD to overestimate the true effect size. Further, we recognize that considerable variation exists both between the RCTs (range 0.4 to 1.5) and the retrospective observational studies (0.75 to 3). For this reason, we would advocate caution in interpreting these values. In particular, the effect size of Kumar and Gowda's<sup>23</sup> study appears excessively large, and therefore more significance might arguably be ascribed to the effect sizes from the much larger<sup>22</sup> or randomized<sup>18,19</sup> studies included in the review. Allowing for this, the data support that CTFESI has a moderate-significant effect on patient-reported outcomes, though studies using a control group are necessary to confirm this.

No reports of serious complications satisfied our a priori inclusion criteria. Reports of catastrophic complications following steroid injection are largely limited to anecdotal, case report, and medicolegal evidence.<sup>28</sup> A thorough analysis of reported complications was provided in an earlier systematic review and are not repeated here in full. In summary, these include spinal cord infarction, cortical blindness, vertebral artery stroke, cerebral infarction, cerebellar infarction, epidural haematoma, grand mal seizures, Horner's syndrome, and death.<sup>13</sup>

An anonymized survey of members of the American Pain Society (287 responders; 21.4% response rate) reported 78 serious complications, including 30 cases of spinal cord or vertebrobasilar infarct and 13 deaths.<sup>29</sup> It is unclear what total number of CTFESIs these complications were drawn from, the procedural volume of the participants, and which techniques or preparations were used, which therefore limits the generalizability of such data. Finally, the sampling/non-response bias, given the low response rate, raises further concerns. In this systematic review, which we believe assesses the best available contemporary evidence, no major complications were encountered. There was a 1.35% incidence of minor, transient complications.

Catastrophic central nervous sequelae as adverse effects following CTFESI are likely to be the result of insult to the posterior cerebral circulation via the vertebral artery, or to the spinal cord via an intraforaminal radicular artery. Lesions therefore result from vascular trauma, vasospasm, or embolic events.<sup>28,30</sup> The latter are associated with the use of particulate steroids, with the injection provoking erythrocyte aggregation and embolization rather than embolism of the particles themselves.<sup>31,32</sup> A growing body of evidence supports the superior safety profile of non-particulate preparations. As a result,

although the literature remains equivocal in considering the efficacy of non-particulate preparations compared to particulate steroid, use of a non-particulate preparation should be considered whenever CTFESI is performed.<sup>33–35</sup> Such a position has been adopted by a number of national bodies, including the USA Food and Drug Administration Safe Use Initiative,<sup>28</sup> and specialist societies such as the British Pain Society and the Faculty of Pain Medicine in association with the Royal College of Anaesthetists.<sup>36</sup> The reports of catastrophic complications cannot be ignored, and patients must be thoroughly counselled regarding the possible risks and benefits of injections during a comprehensive informed consenting process. However, the best available evidence does not replicate the findings of the uncontrolled case reports and survey data, but rather suggests that CTFESI is only associated with a low incidence of minor, transient complications.

There are several limitations to our study. The most important is the lack of a high level of evidence in the studies informing our research question, and the variability in reporting that prevents robust synthesis of the data. There is a lack of detail regarding the indication for CTFESI. The severity of the radiological findings, chronicity of the complaints, and the presence of degenerative changes elsewhere in the cervical spine are three examples of variables for which ideally there would have been control or adjustment. Regarding the incidence of catastrophic complications, we recognize that there may be a significant publication bias confounding the literature. Even within our narrow inclusion criteria, there is variability in technique, and we recognize that including several imaging methods could appear to limit the generalizability of our results, although the findings attributable to each can be considered separately, thus mitigating this. Nonetheless, we believe the highlighted studies offer the best available contemporary evidence describing the role of CTFESI for cervical radicular symptoms.

More work is needed regarding the efficacy and safety of CTFESI and its role in clinical practice. We recognize that RCTs represent the best evidence and would encourage them to be performed, but recognize the literature also lacks much information about significant complications. The sample size of a RCT required to sufficiently power a study to comment confidently on catastrophic complication rates is likely to be prohibitive. As a result, high-quality non-randomized observational studies are needed to raise the level of evidence available to inform both policy and clinical decision-making. We note that studies using a control or placebo group are lacking in the literature.

We are also critical of the heterogeneity of reporting in the contemporary literature. As the most robust source of quality evidence requires data synthesis and meta-analysis across a number of methodologically sound studies, there is increasingly a move to develop standardized ‘core outcome sets’ to facilitate this.<sup>37</sup> Our own experience has highlighted that even with comparatively narrow inclusion criteria, the CTFESI literature demonstrates highly variable reporting which, in our study, prevented comprehensive synthesis of the available data. There have been recent efforts to validate a core outcome set for

cervical radicular syndromes, and we support further validation of this or a similar outcome set.<sup>38</sup>

We consider that further work on the natural history of radiculopathy, and on the prognostic indicators that inform its clinical course, will also be helpful in determining the role of CTFESI in modern practice. Finally, we recognize that the potential valuable role of CTFESI as a diagnostic aid was not explored in our present review.

In conclusion, there is emerging evidence to support the clinical efficacy of CTFESI. The majority of included studies showed improvement following CTFESI which exceeds the MCID of cervical decompressive surgery. Concerns regarding the occurrence of catastrophic complications, widely shared in case reports and anecdotal literature, are not replicated by review of the best available clinical evidence.



### Take home message

- There is emerging evidence supporting the clinical efficacy of cervical transforaminal epidural steroid injections for radicular pain.

- Concerns regarding the occurrence of catastrophic complications are not replicated by review of the best available clinical evidence.

- The strength of these findings remains limited by the lack of highly powered high-level studies and the heterogeneity of the studies available.

### Supplementary material



Proformas used to facilitate review at the abstract and full-text screening stages.

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