



Outcomes of epidural steroids following percutaneous transforaminal endoscopic discectomy: a meta-analysis and systematic review

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Background: Percutaneous transforaminal endoscopic discectomy (PTED) has been widely used in the treatment of lumbar degenerative diseases. Epidural injection of steroids can reduce the incidence and duration of postoperative pain in a short period of time. Although steroids are widely believed to reduce the effect of surgical trauma, the observation indicators are not uniform, especially the long-term effects, so the problem remains controversial. Therefore, the purpose of this paper was to evaluate the efficacy of epidural steroids following PTED.

Methods: We searched PubMed, Embase, and the Cochrane Database from 1980 to June 2021 to identify randomized and non-randomized controlled trials comparing epidural steroids and saline alone following PTED. The primary outcomes included postoperative pain at least 6 months as assessed using a visual analogue scale (VAS) and the Oswestry Disability Index (ODI). The secondary outcomes included length of hospital stay and the time of return to work.

Results: A total of 451 patients were included in three randomized and two non-randomized controlled trials. The primary outcomes, including VAS and ODI scores, did not differ significantly between epidural steroids following PTED and saline alone. There were no significant intergroup differences in length of hospital stay. Epidural steroids were shown to be superior in terms of the time to return to work ($P < 0.001$).

Conclusions: Intraoperative epidural steroids did not provide significant benefits, leg pain control, improvement in ODI scores, and length of stay in the hospital, but it can enable the patient to return to work faster.

Key Words: Discectomy, Percutaneous; Endoscopy; Injections, Epidural; Lumbar Vertebrae; Meta-Analysis; Pain, Postoperative; Saline Solution; Steroids; Systematic Review; Visual Analog Scale.

INTRODUCTION

Pain in the back and legs, after a lumbar disc herniation (LDH), results from an inflammatory process caused by

compression and lumbar herniation [1,2]. Lumbar discectomy can relieve the herniated nucleus pulposus from compressing the nerve, but the edema and inflammation of the nerve will exist for a few days. Inflammatory ir-

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ritation and surgical procedures may cause fibrosis, and negatively affect long-term results, which is believed to cause delayed recurrence of pain [3-5]. Patients who have undergone percutaneous transforaminal endoscopic discectomy (PTED) will recover faster after the operation, because the operation is minimally invasive, with small incisions to, as much as possible, preserve the normal anatomical structure of the lower back muscles and to avoid excessive damage [6-8].

Recently, PTED has become a standard treatment for LDH [9,10]. Since steroids play an important role in reducing inflammation and blocking afferent C fiber damage, as well as causing inflammation of the vascular response, many studies have explored whether steroids can reduce local inflammation and further peridural scar formation after open lumbar discectomy [11-16]. However, a consensus has not yet been reached as to whether or not to use steroids in PTED. At present, there is almost no research in the literature that demonstrates that local injection of steroids during PTED can effectively relieve postoperative pain and reduce its duration. The primary purpose of this study is to compare the long-term outcomes reported when saline or steroids are used in PTED.

MATERIALS AND METHODS

1. Data sources and search strategies

Two researchers independently conducted a comprehensive search of the PubMed, Embase, and the Cochrane Library from 1980 to June 2021. They searched for studies that referring to LDH patients treated with PTED, using the key words “epidural space”, “steroids”, “lumbar vertebrae”, together with “percutaneous”, “endoscopes”, and “discectomy”. The cohort studies associated with epidural steroids embedding for PTED were included. We had no language restrictions in this search. **Appendix** details the search strategy. We registered the protocol of the systematic review on PROSPERO (CRD42021269739).

2. Inclusion and exclusion criteria

Studies that met the following selection criteria were included in the meta-analysis: (1) The study was a cohort study. (2) The subjects of the study were adults with LDH. (3) The study group included an epidural hormone group and a control group. (4) They reported at least one outcome indicator of the visual analogue scale (VAS), Oswestry Disability Index (ODI), length of hospital stay, and time until return to work.

The exclusion criteria were: (1) Previous lumbar spine

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Keorochana et al., 2018 [19]	⊕	⊕	⊕	⊕	⊕	⊕	⊕
Wu et al., 2017 [21]	⊕	⊕	⊕	⊕	⊕	⊕	⊕
Shin et al., 2015 [20]	⊕	⊕	⊕	⊕	⊕	⊕	⊕

Fig. 1. Risk of bias assessment using the Cochrane risk of bias tool for randomized controlled trials included in a meta-analysis.

surgery or lumbar spine fracture surgery; patients with severe trauma, infection, or cancer; reviews, animal studies, and case reports. (2) The last follow-up time was less than six months. (3) The study data could be used for statistical analysis.

3. Data extraction and quality assessment

We extracted the following data from the included studies: name of the first author, publication year, study type, sample size, follow-up period, age and sex of the study population, steroid type, treatment method, and reported outcome indicators. In addition, Cochrane Collaboration’s bias risk assessment tool was used to assess the quality of the randomized controlled trials (RCTs). A quality judgment for retrospective cohort studies (RCSs) was performed with the Newcastle-Ottawa scale. The quality assessment of the RCTs and RCSs are shown in **Fig. 1** and **Table 1**, respectively.

4. Statistical analysis

RevMan 5.3 (The Nordic Cochrane Centre for The Cochrane Collaboration, Copenhagen, Denmark) was used for the meta-analysis. For binary variables, we use the odds ratio and a 95% confidence interval (CI) to evaluate statistics. For continuous variables, we use weighted mean difference and its 95% CI for analysis. A *P* value < 0.05 is assigned statistical significance. The heterogeneity of data

Table 1. Quality assessment of retrospective cohort studies in the meta-analysis based on the Newcastle-Ottawa scale

Study	Selection			Comparability			Outcome			Total scores	Quality
	Exposed cohort	Non-exposed cohort	Ascertainment of exposure	Outcome of interest	The most important factor	Additional factor	Assessment of outcome	Length of follow up	Adequacy of follow up		
Yang et al., 2020 [23]	☆	★	★	★	★	★	★	★	★	8	Good
Hu et al., 2018 [22]	★	★	★	★	★	☆	★	★	★	8	Good

White star: The research isn't according with this point, Black star: The research is according with this point.

was interpreted through I^2 statistic. If $I^2 > 50\%$, a random effects model was used for analysis. If I^2 was less than 50%, the homogeneity of the included study could be considered. Normal distribution was assumed for continuous outcomes, and the interquartile ranges were converted to standard deviation [17,18].

RESULTS

1. Search results and study characteristics

A flowchart of the literature search and selection is shown in Fig. 2. Searches of the databases resulted in 854 articles. Eight hundred thirty-seven articles were excluded after the titles and abstracts were reviewed; 17 articles remained for additional screening. Finally, 12 full-text articles were retrieved, in which 3 RCTs [19-21] and 2 RCSs [22,23] qualified for inclusion. Our meta-analysis included 451 patients (226 patients who underwent epidural steroid treatment during spinal endoscopy and 225 patients who received normal saline treatment). The characteristics of the study are shown in Table 2. All research outcome indicators were followed up for at least six months.

2. Comparison of epidural steroids vs. saline alone

1) VAS score for leg pain

Four studies [19-22] reported the VAS score for postoperative leg pain. A total of 356 patients were enrolled, and the patients who received epidural steroid treatment and normal saline treatment were equally divided. Postoperative scores ($P = 0.38$; mean difference [MD], -0.07; 95% CI, -0.22 to 0.09; $I^2 = 0\%$; Fig. 3) were not statistically significant in the epidural steroids group and saline group.

2) VAS score for lumbar pain

Three studies [19,20,22] used the VAS score of postoperative low back pain as a prognostic indicator. There were 230 patients in total, including 115 patients in the epidural steroid group and 115 patients in the normal saline group. There was no significant difference between the epidural steroid and saline groups ($P = 0.37$; MD, -0.12; 95% CI, -0.39 to 0.14; $I^2 = 11\%$; Fig. 4).

3) Postoperative ODI

Three studies [19,20,22] evaluated postoperative ODI scores, and a total of 230 patients included 115 patients in the epidural steroid group and 115 patients in the saline

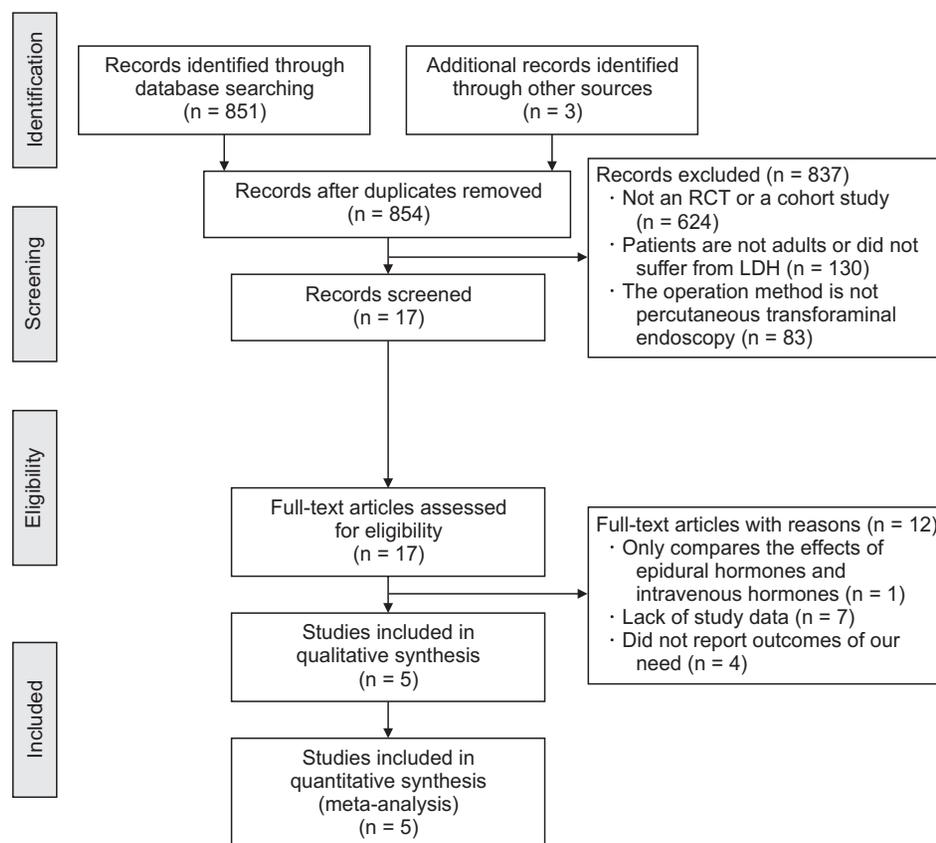


Fig. 2. Flow chart illustrating the study selection process. RCT: randomized controlled trial, LDH: lumbar disc herniation.

group. No statistical difference was found in the postoperative ODI comparison between the two groups ($P = 0.87$; MD, 0.37; 95% CI, -4.07 to 4.80; $I^2 = 73\%$; Fig. 5).

4) Time of hospital stay (days)

Hospitalization days were analyzed in 3 studies [20,21,23], including 161 patients in the epidural steroids group and 160 patients in the saline group. The results showed that there was no statistical difference between the two groups ($P = 0.10$; MD, -0.93; 95% CI, -2.06 to 0.19; $I^2 = 97\%$; Fig. 6).

5) Time to return to work

Three studies [20,21,23] recorded the time to return to work, including 161 patients in the epidural steroids group and 160 patients in the saline group. The results of this meta-analysis showed that the time to resuming work in the epidural steroid group was significantly lower than that in the normal saline group, with significant statistical differences ($P < 0.001$; MD, -1.17; 95% CI, -1.34 to -1.00; $I^2 = 0\%$; Fig. 7).

DISCUSSION

Meta-analysis currently published [24-26] showed that it is safe to inject epidural steroids during lumbar spine surgery. According to the search, there was no meta-analysis on the outcomes of using epidural steroids after PTED, so this study is the first. The VAS score (leg or lumbar), postoperative ODI score after at least six months of follow-up, and time of hospital stay did not show any statistical difference. However, there was a significant difference in the performance of the two groups in their time to resuming work.

Our study did not find that epidural injection can more effectively reduce the VAS score (leg or lumbar) after six months compared with the control group. For our meta-analysis, we chose the last score in the study, although differences in VAS assessment time may influence our results. The time until return to work with the epidural steroids group was significantly lower than the saline group. The meta-analysis shows that epidural steroid injections can allow patients to return to work faster. The time to return to work reflects the short-term relief of the patient's back and leg pain. However, the difficulty in maintaining employment, unemployment, and economic status are highly influential when deciding to return to work after an operation. Many studies have used the ODI in assess-

Table 2. The characteristics of the studies included in this meta-analysis

Study	Level of study	Group	Follow up time	Sex (M/F)	Age (yr)	Epidural injection	Outcomes
Yang et al., 2020 [23]	Retrospective	Epidural steroids	1 yr	28/22	34.8 (17-59)	A mixture of ropivacaine, dexamethasone and vitamin B12	VAS, ODI, the mean hospital stay time, returned to work time, the modified MacNab criteria
Keorochana et al., 2018 [19]	RCT	Control	6 mo	27/23	35.3 (18-61)	Saline	24-hour morphine consumption, VAS, ODI, Roland-Morris Disability Questionnaire score, and complications
	Epidural steroids	A mixture of triamcinolone and saline					
Hu et al., 2018 [22]	Retrospective	Control	1 yr	36/24	41.3 ± 8.7	Saline	VAS, ODI
		Epidural steroids				A mixture of dexamethasone (40 mg) with 5% glucose injection	
Wu et al., 2017 [21]	RCT	Control	6 mo	33/30	41.20 ± 15.10	Saline	VAS, ODI, the mean hospital stay time, returned to work time, the modified MacNab criteria
		Epidural steroids				A mixture of compound betamethasone, lidocaine and mecobalamin	
Shin et al., 2015 [20]	RCT	Control	26 wk	21/29	34.52 (19-57)	Saline	VAS, ODI, the mean hospital stay time, returned to work time
		Epidural steroids				A mixture of triamcinolone and saline	
		Control		19/31	35.84 (18-61)	Saline	

Values are presented as number only, mean (range), or mean ± standard deviation.
 RCT: randomized controlled trial, VAS: visual analogue scale, ODI: Oswestry Disability Index.

ing the degree of dysfunction in patients with LDH [27,28]. Our study did not find a statistically significant difference in postoperative ODI scores between the epidural steroid group and the normal saline group.

Ranguis et al. [14] conducted a meta-analysis of the articles found and searched the database for the effects of epidural steroids during the perioperative period. They reported that epidural steroids could relieve pain in patients undergoing lumbar spine surgery caused by LDH or lumbar spinal stenosis in a short period. Wilson-Smith et al. [24] conducted a study that included 17 RCTs on the effect of epidural steroids during closure after minimally invasive discectomy or laminectomy. They found that intraoperative or perioperative epidural injection of steroids can benefit pain control, shorten hospital stays, and reduces use of opioid analgesia after surgery.

Although many patients have undergone lumbar spine surgery, they continue to experience back and leg pain. There are many reasons for these symptoms, including insufficient resection of the lesion, lack of rehabilitation, misdiagnosis or complications (such as arachnoiditis and recurrence of the nucleus pulposus protrusion), epidural scar, or infection. For lumbar degenerative diseases, epidural steroids are widely used to relieve preoperative pain or postoperative acute pain. The use of steroids can inhibit the release of inflammatory mediators, such as the effects of prostaglandins, bradykinin, and histamine [29-31].

Inflammation has been proven to play an important role in causing pain between the damaged disc tissue and peripheral nerve tissue [32,33]. According to reports, about half of surgeons routinely use epidural steroids after surgery [34]. Some studies have reported that patients receiving epidural steroids after lumbar spine surgery have increased infection rates, leading to epidural abscesses [35]. However, some meta-analysis studies [25] have shown that the use of epidural steroids in lumbar spine surgery can increase the likelihood of infection, but no statistical significance has been shown.

Compared with epidural injection in open LDH surgery, percutaneous intervertebral foraminal endoscopy has many advantages. First of all, direct endoscopic vision can ensure that epidural infusion is safe and effective. Drugs can be delivered to the epidural space through endoscopy without puncturing the dural sac. Second, the drug can be injected into the dural sac and the ventral side of the nerve root. Third, the drug is not easy to lose in a closed space and can maintain efficacy for a long time. Lee and Lee [36] showed that injecting medications into the ventral side of the nerve can improve the therapeutic effect of epidural injection. In traditional open surgery of the lumbar intervertebral disc, the drug is usually injected into the dorsal side of the nerve, where the drainage tube needs to be

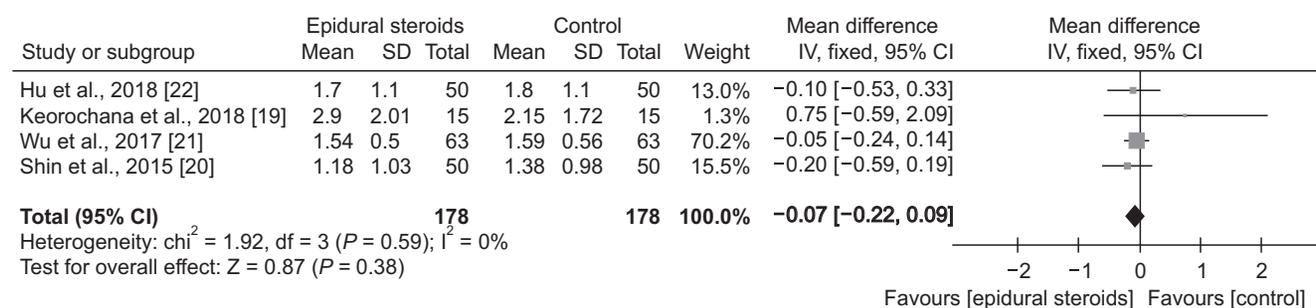


Fig. 3. Forest plot of postoperative visual analogue scale scores for leg pain in a meta-analysis on the efficacy of epidural steroids and saline alone for percutaneous transforaminal endoscopic discectomy. SD: standard deviation, IV: inverse variance, CI: confidence interval, df: degree of freedom.

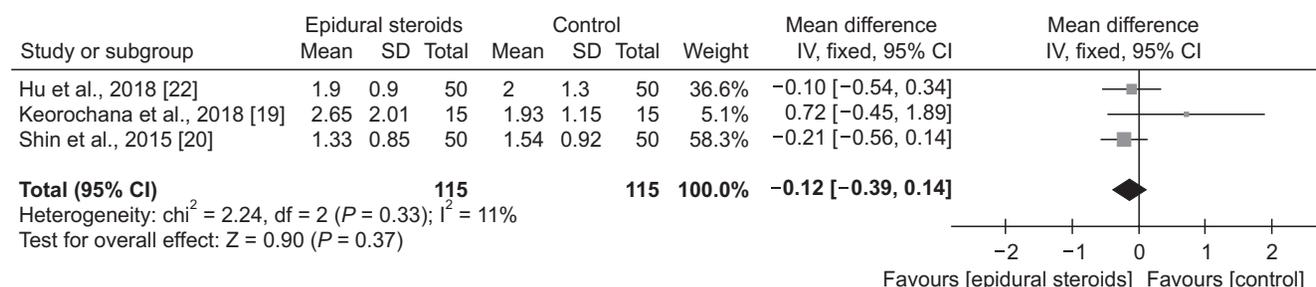


Fig. 4. Forest plot of postoperative visual analogue scale scores for lumbar pain in a meta-analysis on the efficacy of epidural steroids and saline alone for percutaneous transforaminal endoscopic discectomy. SD: standard deviation, IV: inverse variance, CI: confidence interval, df: degree of freedom.

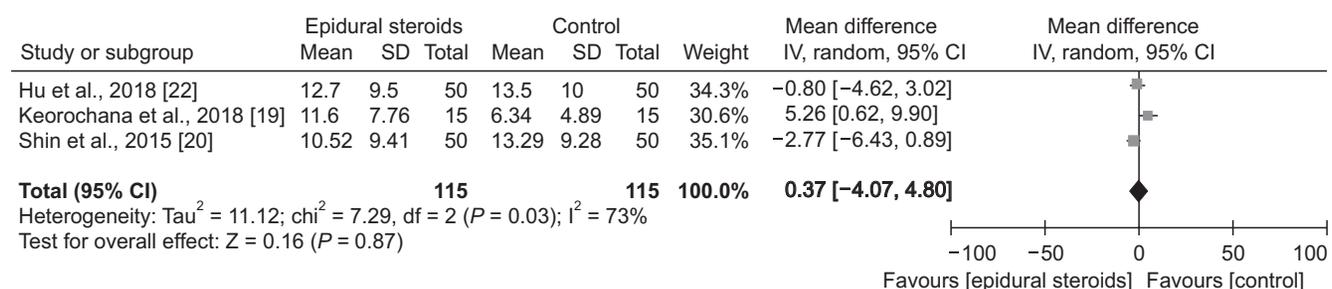


Fig. 5. Forest plot of postoperative Oswestry Disability Index in a meta-analysis on the efficacy of epidural steroids and saline alone for percutaneous transforaminal endoscopic discectomy. SD: standard deviation, IV: inverse variance, CI: confidence interval, df: degree of freedom.

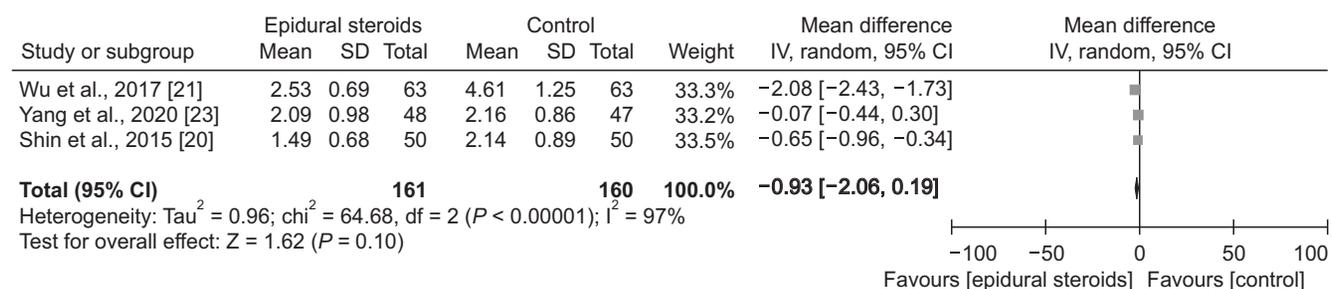


Fig. 6. Forest plot of time of hospital stay in a meta-analysis on the efficacy of epidural steroids and saline alone for percutaneous transforaminal endoscopic discectomy. SD: standard deviation, IV: inverse variance, CI: confidence interval, df: degree of freedom.

placed, resulting in drug loss.

This meta-analysis has some limitations. First, there are few cohort studies that meet the inclusion criteria and only include 3 RCTs. Second, 2 RCTs were included, which

could cause a significant risk of selection and reporting bias [37,38]. Third, the type and ratio of steroids in each study, and the time of follow-up end point are different, and some studies lack relevant indicators. Finally, most

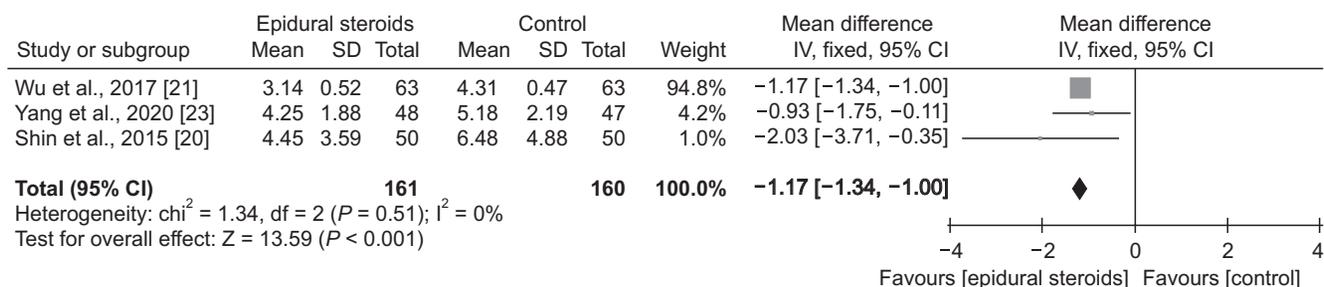


Fig. 7. Forest plot of time of return to work in a meta-analysis on the efficacy of epidural steroids and saline alone for percutaneous transforaminal endoscopic discectomy. SD: standard deviation, IV: inverse variance, CI: confidence interval, df: degree of freedom.

of the included studies were relatively small sample sizes and from a single site, affecting generalizability. More extensive and well-defined RCTs would increase predictive strength.

In conclusion, intraoperative epidural steroids did not provide significant improvements in leg pain control, ODI score, and length of hospital stay, but it did allow the patient to return to work faster. It is hoped that there will be more high-quality RCTs to confirm the long-term effect of hormones in percutaneous lumbar foraminal endoscopy.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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Appendix. Search strategy

PubMed

- #1 epidural space[MeSH Terms]
- #2 steroids[MeSH Terms]
- #3 #1 AND #2
- #4 (“epidural”[All Fields] AND “space”[All Fields]) OR “epidural space”[All Fields] OR “epidural”[All Fields] OR “epidurally”[All Fields] OR “epidurals”[All Fields]) AND (“steroidal”[All Fields] OR “steroidals”[All Fields] OR “steroidic”[All Fields] OR “steroids”[All Fields] OR “steroid”[All Fields])
- #5 “Lumbar Vertebrae”[Mesh]
- #6 Vertebrae, Lumbar[Title/Abstract]
- #7 “diskectomy”[MeSH Terms]
- #8 “Interlaminar”[All Fields] AND (“diskectomy”[MeSH Terms] OR “diskectomy”[All Fields] OR “discectomies”[All Fields] OR “discectomy”[All Fields])
- #9 #4 OR#5 OR#6 OR#7 OR#8
- #10 #3 OR #9
- #11 (“percutaneous”[All Fields] OR “percutaneously”[All Fields] OR “percutaneous”[All Fields]) AND (“endoscope s”[All Fields] OR “endoscoped”[All Fields] OR “endoscopes”[MeSH Terms] OR “endoscopes”[All Fields] OR “endoscope”[All Fields] OR “endoscopical”[All Fields] OR “endoscopically”[All Fields] OR “endoscopy”[MeSH Terms] OR “endoscopy”[All Fields] OR “endoscopic”[All Fields]) AND “Interlaminar”[All Fields] AND (“diskectomy”[MeSH Terms] OR “diskectomy”[All Fields] OR “discectomies”[All Fields] OR “discectomy”[All Fields])
- #12 randomized controlled trial[Publication Type] OR randomized[Title/Abstract] OR placebo[Title/Abstract]
- #13 #10 AND#11 AND#1

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- #1 epidural space[MeSH Terms]
- #2 steroids[MeSH Terms]
- #3 #1 AND #2
- #4 (“epidural”[All Fields] AND “space”[All Fields]) OR “epidural space”[All Fields] OR “epidural”[All Fields] OR “epidurally”[All Fields] OR “epidurals”[All Fields]) AND (“steroidal”[All Fields] OR “steroidals”[All Fields] OR “steroidic”[All Fields] OR “steroids”[All Fields] OR “steroid”[All Fields])
- #5 #3 OR #4
- #6 (“percutaneous”[All Fields] OR “percutaneously”[All Fields] OR “percutaneous”[All Fields]) AND (“endoscoped”[All Fields] OR “endoscopes”[MeSH Terms] OR “endoscopes”[All Fields] OR “endoscope”[All Fields] OR “endoscopical”[All Fields] OR “endoscopically”[All Fields] OR “endoscopy”[MeSH Terms] OR “endoscopy”[All Fields] OR “endoscopic”[All Fields])
- #7 “diskectomy”[MeSH Terms] OR “diskectomy”[All Fields] OR “discectomies”[All Fields] OR “discectomy”[All Fields]
- #8 “Lumbar Vertebrae”[Mesh] OR Lumbar[Title/Abstract]
- #9 #5 AND #6 AND #7 AND 8

Embase

- 1 (epidural or epidural space or epidural or epidurally or epidurals).af.
- 2 (steroidal or steroidals or steroidic or steroids or steroid).af.
- 3 1 and 2
- 4 (percutaneous or percutaneously or percutaneous).af.
- 5 (endoscoped or endoscopes or endoscope or endoscopical or endoscopically or endoscopy or endoscopic).af.
- 6 4 and 5
- 7 (diskectomy or discectomies or discectomy).af.
- 8 lumbar.ab.
- 9 3 and 6 and 7 and 8