5-1-2018

Corticosteroid Administration to Prevent Complications of Anterior Cervical Spine Fusion: A Systematic Review.

Shayan Abdollah Zadegan
Tehran University of Medical Sciences

Seyed Behnam Jazayeri
Tehran University of Medical Sciences

Aidin Abedi
Tehran University of Medical Sciences

Hirbod Nasiri Bonaki
Tehran University of Medical Sciences

Alexander R. Vaccaro
Thomas Jefferson University

Review Article

AOSPINE

Global Spine Journal
2018, Vol. 8(3) 286-302

DOI: 10.1177/2192568217708776
journals.sagepub.com/home/gsj
SAGE

Corticosteroid Administration to Prevent Complications of Anterior Cervical Spine Fusion: A Systematic Review

Shayan Abdollah Zadegan, MD[1], Seyed Behnam Jazayeri, MD[1], Aidin Abedi, MD[1], Hirbod Nasiri Bonaki, MD[1], Alexander R. Vaccaro, MD, PhD[2], and Vafa Rahimi-Movaghar, MD[1]

Abstract

Study Design: Systematic review.

Objectives: Anterior cervical approach is associated with complications such as dysphagia and airway compromise. In this study, we aimed to systematically review the literature on the efficacy and safety of corticosteroid administration as a preventive measure of such complications in anterior cervical spine surgery with fusion.

Methods: Following a systematic literature search of MEDLINE, Embase, and Cochrane databases in July 2016, all comparative human studies that evaluated the effect of steroids for prevention of complications in anterior cervical spine surgery with fusion were included, irrespective of number of levels and language. Risk of bias was assessed using MINORS (Methodological Index for Non-Randomized Studies) checklist and Cochrane Back and Neck group recommendations, for nonrandomized and randomized studies, respectively.

Results: Our search yielded 556 articles, of which 9 studies (7 randomized controlled trials and 2 non–randomized controlled trials) were included in the final review. Dysphagia was the most commonly evaluated complication, and in most studies, its severity or incidence was significantly lower in the steroid group. Although prevertebral soft tissue swelling was less commonly assessed, the results were generally in favor of steroid use. The evidence for airway compromise and length of hospitalization was inconclusive. Steroid-related complications were rare, and in both studies that evaluated the fusion rate, it was comparable between steroid and control groups in long-term follow-up.

Conclusions: Current literature supports the use of steroids for prevention of complications in anterior cervical spine surgery with fusion. However, evidence is limited by substantial risk of bias and small number of studies reporting key outcomes.

Keywords

cervical vertebrae, diskectomy, intervertebral disc, spinal fusion, steroids

Introduction

The anterior approach to the cervical spine using Smith-Robinson technique has been commonly used for the treatment of cervical discopathies.[1,2] Although the anterior approach is believed to be a relatively safe and effective procedure, it has been associated with complications such as dysphagia, dysphonia, airway compromise, and other tissue injuries.[3-6]

Dysphagia is an unpleasant condition and the most common complication after anterior cervical approach with a reported incidence rate of 1% to 79%, starting early in the postoperative course.[7-9] Although the etiology of dysphagia after anterior cervical spine surgery is not fully understood and there are many discrepancies in the findings of various studies, some factors such as local tissue edema, recurrent laryngeal nerve palsy,

[1] Tehran University of Medical Sciences, Tehran, Iran
[2] The Rothman Institute at Thomas Jefferson University, Philadelphia, PA, USA

Corresponding Author:
Vafa Rahimi-Movaghar, Sina Trauma and Surgery Research Center, Hassan Abad Square, Imam Khomeini Street, PO Box 11365/3876, Tehran, Iran.
Email: V_rahimi@sina.tums.ac.ir

retraction of midline structures during the surgery, and prevertebral soft tissue swelling (PSTS) have been proposed.[7,10]

Airway compromise is the most serious complication, associated with pharyngeal edema, as well as hematoma, angioedema, cerebrospinal fluid leak, and graft displacement.[11-16] Although a rare complication, airway compromise is life-threatening as it could lead to reintubation, tracheostomy, or death.[5,17]

Corticosteroids are known anti-inflammatory agents that inhibit the production of inflammatory prostaglandins and cytokines. Since major adverse outcomes after anterior approach are attributable to pharyngeal edema, it has been assumed that steroids can reduce the incidence of complications.[5] The aim of this systematic review is to evaluate the current evidence regarding the efficacy and safety of steroids in reducing the complications of the anterior cervical spine surgery.

Methods

Protocol

This systematic review was designed according to the guidelines of Cochrane Handbook for Systematic Reviews of Interventions (v. 5.1.0),[18] method guideline for systematic reviews in the Cochrane Back and Neck (CBN) group [formerly Cochrane Back Review Group (CBRG)],[19,20] and the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA)[21-23] statement.

Eligibility Criteria

We included all studies with a control group including randomized controlled trials (RCTs), controlled clinical trials, cohort studies, and case-control studies. The target population was patients of any age who underwent anterior cervical discectomy and fusion (ACDF) or anterior cervical corpectomy and fusion with one- or multiple-level fusion and received corticosteroids to prevent complications following the surgery. We excluded studies that used cervical epidural steroid injections as a diagnostic or therapeutic modality to relieve radiculopathy or neck pain before the surgery. Animal studies were also excluded.

Literature Search and Information Sources

We performed a systematic search of the literature on July 10, 2016, using the following electronic databases without any restrictions on language or date of publications: MEDLINE (via OvidSP and PubMed), Embase, and Cochrane EBM (CENTRAL, DSR, and DARE). The complete search strategy is presented in the appendix. Main search keywords were "anterior," "cervical vertebrae," "cervical," "neck," "intervertebral disc," "spinal decompression," "disc degeneration," "disc displacement," "disc herniation," "radiculopathy," "myelopathy," "spinal fusion," "arthrodesis," "discectomy," "glucocorticoids," and "steroids." Unpublished records were not considered in this review.

Study Selection

Two authors (SAZ and SBJ) screened all titles and abstracts independently. Full texts of relevant articles were obtained and assessed for eligibility. To select the articles, we used a discussion and consensus method at each step, and in case of disagreement, a third reviewer (AA) was consulted. We also screened the reference lists of included articles and relevant reviews for possible inclusions.

Data Items and Collection Process

Two independent reviewers (SAZ and SBJ) used a predetermined form to extract the following information: study design, type of anterior procedure, demographic information, number of operated levels, inclusion/exclusion criteria for each study, dosage of the corticosteroid drug, and outcome variables. The rate of disagreement between the 2 extractors was 1%.

Outcome variables considered in this review were dysphagia/odynophagia, PSTS, airway compromise, length of hospital stay, steroid-related complications, and fusion rate.

Risk of Bias

The risk of bias was independently assessed by 2 authors (SAZ and SBJ). Disagreements were resolved with consensus or consultation with a third reviewer (AA). For randomized studies, we used the 13-item criteria recommended by the Cochrane Back and Neck (CBN).[19,20] This tool contains 5 domains of bias, including selection bias (criteria 1, 2, and 9), performance bias (criteria 3, 4, 10, and 11), detection bias (criteria 5 and 12), attrition bias (criteria 6 and 7), and reporting bias (criterion 8). There is also a 13th criterion, which covers any potential bias that is not detected with previous items.[20] For nonrandomized studies, the 12-item criteria of Methodological Index for Non-Randomized Studies (MINORS) were used.[24] Each criterion is scored from 0 to 2, and the highest possible score for comparative studies is 24. This tool is proved to be valid and reliable to evaluate interventional studies.[24-26]

A pilot test of the risk of bias assessment was performed on a set of similar articles. The Review Manager (RevMan) Version 5.3 (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014) was used for assessment of the risk of bias and production of related tables.

Data Synthesis

Meta-analysis was not feasible due to the heterogeneity of studies.

Results

Study Selection

Our search yielded 556 results. Six additional titles were identified through hand-searching of the reference lists (Figure 1). Of the 31 full-text articles included in the primary screening

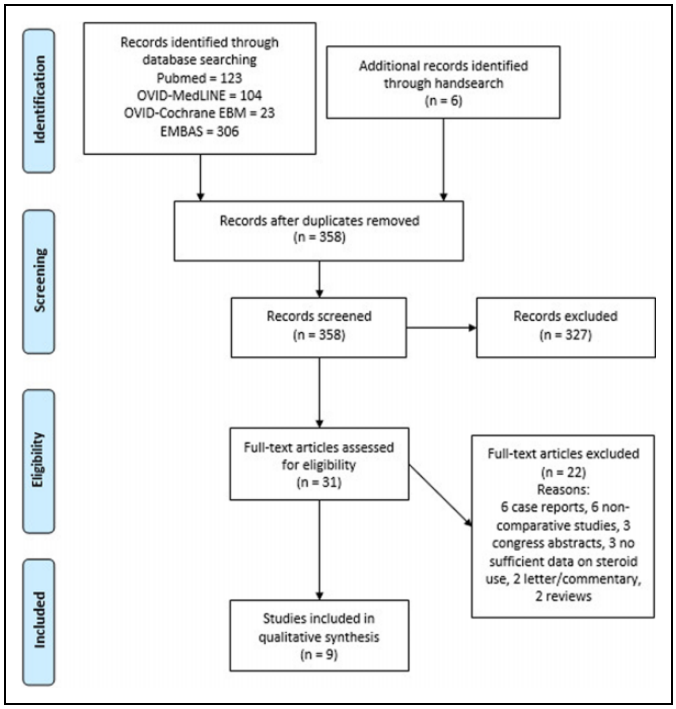


Figure 1. PRISMA flow diagram.

stage, 9 studies (total population: 246 414) were eligible for further consideration: 7 RCTs[16,27-32] and 2 nonrandomized studies (one cohort[33] and one case-control study[34]). The other 22 articles were excluded because they were case reports,[13,35-39] studies without a control group for steroid,[40-45] seminar abstracts,[46-48] reviews,[49,50] commentaries,[51,52] or studies without sufficient data on steroid use.[53-55] Table 1 shows characteristics of the included studies.

Risk of Bias

We assessed the risk of bias for 7 randomized studies with CBN criteria (Figure 2). The 2 extractors primarily disagreed on 14 out of 91 items, all of which were consequently resolved through discussion and consensus. Allocation concealment, random sequence generation, and blinding (especially personnel and outcome assessors) were reported in less than 50% of the trials (Figure 3).

We used MINORS tool for the 2 nonrandomized studies (Figure 4). Of the total 24 items, 4 items required further discussion and consultation with a third reviewer. Blind evaluation of the endpoints (item 5), loss to follow-up (item 7), and prospective calculation of the study size (item 8) were not addressed in both studies.

Outcomes

A detailed summary of the outcome measures is presented in Table 2.

Dysphagia/Odynophagia

In this series of studies, main assessment tools for dysphagia/odynophagia were the following:

1. Bazaz scale, which has 4 grades including none (no dysphagia), mild (rare episodes of dysphagia with solid food), moderate (occasional difficulty swallowing foods such as bread or meat), and severe (frequent dysphagia with liquids and majority of foods).[8] The Bazaz scale has been widely used because of its simplicity; however, it has never been validated.[56] Among included studies, Song et al[30] and Koreckij et al[34] used this scale, and Edwards et al[32] applied a modified version.
2. Eating Assessment Tool (EAT-10), a 10-item questionnaire with 0 to 4 points for each item (0 = no problem, 4 = severe problem) and maximum total of 40 points. A total score greater than 3 is indicative of dysphagia.[57] Koreckij et al[34] used this tool besides the Bazaz scale.
3. Functional Outcome Swallowing Scale (FOSS) was administered in one study by Jeyamohan et al.[31] This scale defines different stages for dysphagia ranging from asymptomatic (stage 0) to non–oral feeding for all nutrition (stage V).[58]
4. The Visual Analogue Scale (VAS) was used by Lee et al[16] and Nam et al[29] for odynophagia.

Five RCTs reported that intravenous or local corticosteroids significantly reduce dysphagia after anterior spinal surgery.[16,27,30-32] Pedram et al[27] performed fiber-optic examination of the oropharynx, the hypopharynx, and the larynx. They found that pharyngolaryngeal lesions were significantly more severe in the control group during the first 36 hours after surgery. Lee et al[16] reported a lower VAS for odynophagia immediately after surgery and during the first 2 weeks. Song at al[30] monitored dysphagia with the Bazaz scale for the first 5 days after surgery. Although the severity of dysphagia was the same between the 2 groups in the first day, it was significantly reduced in the steroid group in postoperative days 2 to 5. Similarly, Edwards et al[32] found no significant difference in the modified Bazaz scale between steroid and control groups in the first day postoperative, but afterwards, a significant reduction of symptoms occurred in the steroid group, which remained through the 28 days of follow-up. Jeyamohan et al,[31] in a long-term follow-up (24 months) by FOSS, showed that the severity of dysphagia is significantly lower in the steroid group during the first month.

Of the 2 remaining RCTs, the one by Emery et al[28] did not have data regarding the swallowing problems, and the other by Nam et al[29] showed no significant difference in VAS scores for odynophagia between the control, low-dose, and high-dose steroid groups during the first 5 days after surgery. Their study was the only one that had a population of pure one-level procedure, while all other studies also included multilevel procedures.

Both the nonrandomized studies found positive effects of steroids on reducing the incidence or severity of dysphagia.

Table 1. Characteristics of Included Studies.

Author, Year	Study Design	Procedure	Patients/Levels	Levels	Mean Age, Years (Range)	FU (Range)	Inclusion/Exclusion Criteria	Steroid
Pedram (2003)[27]	Prospective RCT	ACDF, ACCF, Isolated discectomy, Isolated fusion • Plate fixation: Y	236 C:158 S:78	—	C: 47 ± 15.3 (15-88) S: 47 ± 12.3 (17-83)	36 h	Inclusion: patients requiring exclusively anterior operation of the cervical spine	Methylprednisolone (IV), 1 mg/kg at 0, 12, and 24 h postop
Emery (2009)[28]	Prospective RCT	ACCF, 2-4 levels • Fusion: fibular strut graft • Plate fixation: N	66 C: 31 S: 35	II: 24 III: 38 IV: 4	—	—	Inclusion: cervical stenosis with cord compression at multiple levels	Dexamethasone (IV), 0.3 mg/kg before the incision, followed by 0.15 mg/kg at 8 and 16 h later
Lee (2011)[16]	Prospective RCT	ACDF, 1-2 levels • Fusion: PEEK cage filled with autologous cancellous bone • Plate fixation: Y	50 C: 25 S: 25	I: 29 II: 21	C: 50.9 S: 54.3	21.6 m (16-32)	Inclusion: radiculopathy or myelopathy requiring 1- or 2-level ACDF Exclusion: fusion >3 segments, revision surgery, corpectomy, trauma, infection, tumor, general metabolic diseases (such as rheumatoid arthritis, diabetes, and chronic heart and renal diseases)	Triamcinolone (RF), 40 mg in a morcellized collagen sponge
Nam (2013)[29]	Prospective RCT	ACDF, 1 level • Fusion: allogeneic cortical bone and DBM • Plate fixation: Y	62 C: 22 S1: 20 S2: 20	I: 62	C: 48.8 ± 7.6 S1: 45.6 ± 7.3 S2: 46.9 ± 8.6	5 d	Inclusion: cervical radiculopathy requiring single-level ACDF Exclusion: radiculopathy requiring ACDF ≥2 levels, myelopathic disease, cervical trauma, corpectomy	Dexamethasone (IV), S1: 10, 5, 5 mg; S2: 20, 10, 10 mg, at 0, 24, and 48 h postop
Song (2014)[30]	Prospective RCT	ACDF, 3-4 levels • Plate fixation: Y	40 C: 20 S: 20	C III: 10 IV: 10 S III: 10 IV: 10	C: 57.3 ± 11.0 (29-77) S: 59.9 ± 10.3 (42-74)	3 m	Inclusion: degenerative cervical disease requiring multilevel ACDF confirmed with preoperative plain radiographs, computed tomography, and magnetic resonance imaging Exclusion: trauma other than that related to the operative procedure that could influence soft-tissue swelling	Methylprednisolone (IV), 250 mg at 0, 6, 12, and 24 h postop
Jeyamohan (2015)[31]	Prospective RCT	ACDF, 2-5 levels • Fusion: carbon-fiber cage filled with HA, collagen and autologous BMA • Plate fixation: Y	112 C: 56 S: 56	II: 28 III: 40 IV: 42 V: 2	C: 55 S: 54	24 m	Inclusion: age ≥18 y, cervical spondylosis requiring surgical treatment at ≥2 motion segments, ventrally approachable vertebral levels Exclusion: pregnancy, chronic preop steroid use, coma, incapacitation, unable to provide consent, allergy to dexamethasone or related drugs	Dexamethasone (IV), 0.2 mg/kg intraoperative dose followed by 0.06 mg/kg doses at 6, 12, and 24 h later

(continued)

Table 1. (continued)

Author, Year	Study Design	Procedure	Patients/Levels	Levels	Mean Age, Years (Range)	FU (Range)	Inclusion/Exclusion Criteria	Steroid
Edwards (2016)[32]	Prospective RCT	ACDF, 1-3 levels • Fusion: PEEK spacer, local bone graft, and BMP-2 • Plate fixation: Y	50 C: 23 S: 27	C I: 30.4% II: 69.6% S I: 55.6% II: 33.3% III: 11.1%	C: 53.5 S: 54.0	1 m	Inclusion: age 18-70 y, elective 1-, 2-, or 3-level ACDF, primary or revision cases Exclusion: nondegenerative pathology (fracture, tumor, infection, etc), $\geq$4-level ACDF, combined lumbar fusion surgery, circumferential surgical approaches	Methylprednisolone (RF), 40 mg/cc in a 1 $\times$ 3 cm collagen sponge
Cancienne (2016)[33]	Retrospective cohort	ACDF, 1-2 levels	200 000 C: 198 230 S: 1770	—	Age <70 C: 66.8% S: 69.8% Age >80 C: 6.2% S: 5.4%	3 m	Inclusion: ACDF procedures using CPT codes 22554, 22551, 22585, and 63076 in addition to the ICD-9 procedure code 810.2	Local injection of Triamcinolone acetonide, 1 or 10 mg Methylprednisolone acetate, 20 or 40 or 80 mg
		ACDF, $\geq$3 levels	45 754 C: 45 432 S: 322	—	Age <70 C: 61.8% S: 60.1% Age >80 C: 6.3% S: 5.6%			
Koreckij (2016)[34]	Retrospective case-control	ACDF, 2-4 levels • Fusion: Cortical allograft packed with DBM and local bone • Plate fixation: Y	44 C: 22 S: 22	C II: 10 III: 11 IV: 1 S II: 10 III: 11 IV: 1	C: 57.6 $\pm$ 9.9 S: 55.1 $\pm$ 7.9	3 m	Inclusion: ACDF for radiculopathy or myelopathy Exclusion: Single-level procedures, revision surgery, trauma, infection, tumor, autoimmune-related diseases (ie, rheumatoid arthritis)	Methylprednisolone (RF), 80 mg in a morcellized collagen sponge

Abbreviations: ACCF, anterior cervical corpectomy and fusion; ACDF, anterior cervical discectomy and fusion; BMA, bone marrow aspirate; BMP, bone morphogenetic protein; C, control/sham/placebo group; CPT, Current Procedural Terminology; d, day(s); DBM, demineralized bone matrix; FU, follow-up; h, hour(s); HA, hydroxyapatite; ICD-9, International Classification of Disease, 9th Revision; IV, intravenous; m, month(s); N, no; PEEK, polyether ether ketone; RF, retropharyngeal; S, steroid group; Y. yes.

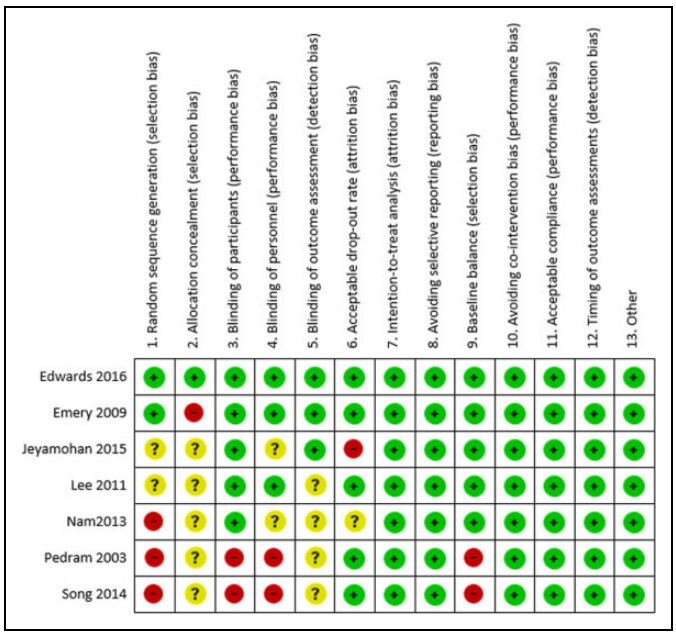


Figure 2. Summary of risk of bias for randomized studies (the 13-item criteria of the Cochrane Back and Neck group): review authors' judgments about each risk of bias items for each included study. Plus sign (green): low risk; Minus sign (red): high risk; Question mark (yellow): unclear risk of bias.

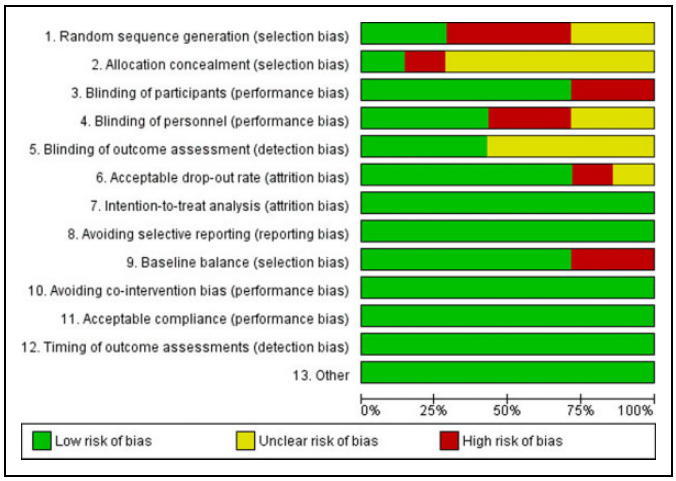
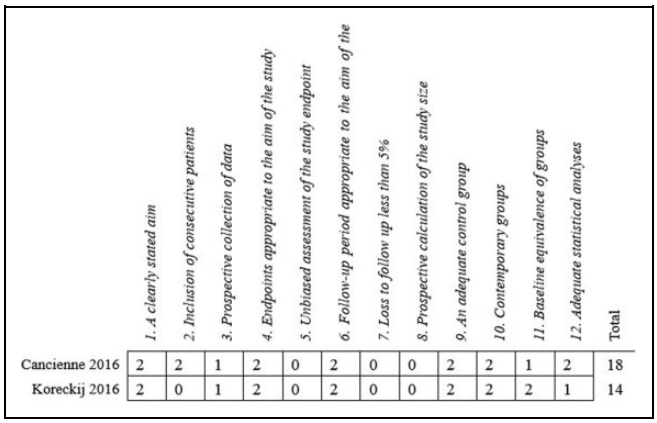


Figure 3. Summary of risk of bias for randomized studies (the 13-item criteria of the Cochrane Back and Neck group): review authors' judgments about each risk of bias items across all included studies.

Cancienne et al[33] in a cohort of 245 754 patients showed that incidence of dysphagia is lower within 90 days postoperatively in patients treated with steroids. However, this finding was only significant in ACDF ≥3-level fusion. Koreckij et al[34] reported a significant reduction in severity of dysphagia with EAT-10 and Bazaz scale at 1.5- and 3-month follow-up.

Prevertebral Soft Tissue Swelling

Only 4 of the included studies reported PSTS and there were variations in their assessment methods. Lee et al[16] calculated



	1. A clearly stated aim	2. Inclusion of consecutive patients	3. Prospective collection of data	4. Endpoints appropriate to the aim of the study	5. Unbiased assessment of the study endpoint	6. Follow-up period appropriate to the aim of the	7. Loss to follow up less than 5%	8. Prospective calculation of the study size	9. An adequate control group	10. Contemporary groups	11. Baseline equivalence of groups	12. Adequate statistical analyses	Total
Cancienne 2016	2	2	1	2	0	2	0	0	2	2	1	2	18
Koreckij 2016	2	0	1	2	0	2	0	0	2	2	2	1	14

Figure 4. Summary of risk of bias for nonrandomized studies (MINORS criteria): review authors' judgments about each risk of bias items for each included study. 0: Not reported; 1: Reported but inadequate; 2: Reported and adequate.

the ratio of the anteroposterior diameter of each vertebral body to the prevertebral soft tissue thickness in lateral radiographs of cervical spine and reported a mean percentage of PSTS at C3-5 as PSTS index. Koreckij et al[34] used the same method; the only difference was that the PSTS index was calculated for C3-7. Nam et al[29] measured the prevertebral soft tissue density, an area of the prevertebral soft tissue (in cm^2) from the lower border of C1 to the upper end plate of C7 in lateral radiographs. Song et al[30] measured the diameter of prevertebral tissue (in mm) in lateral view.

The effect of steroid administration on PSTS was concordant with the findings for dysphagia. Nam et al[29] found no significant difference in PSTS among groups within 5 days postoperative. Lee et al[16] and Song et al[30] found significant reduction in PSTS during the 2-week and 1-week follow-ups, respectively. Similar to the results for dysphagia, Song et al[30] reported a nonsignificant difference just for the first day postoperative and a significant effect afterwards.

The only discordance between the results of dysphagia assessment and PSTS was reported in the case-control study by Koreckij et al,[34] where they found no significant difference in PSTS but a significant reduction of dysphagia between the steroid and control groups.

Airway Compromise

The results for this outcome were very limited and poorly reported. Emery et al[28] used delayed extubation (>1 day) as an indicator of airway compromise and found no significant difference between the control and steroid groups. Edwards et al[32] reported no adverse airway events (prolonged intubation, reintubation, or readmission for breathing difficulty) in the steroid group and only one readmission for breathing difficulty in the control group, which was not statistically significant. Nam et al[29] conducted VAS score for dyspnea. Although they reported no significant effect of steroids on reduction of dysphagia and PSTS, dyspnea was significantly reduced in the

Table 2. Summary of Findings.

Author, Year	Dysphagia/Odynophagia	Prevertebral Soft Tissue Swelling	Airway Compromise	Length of Hospital Stay	Postoperative Steroid Need	Steroid-Related Complications	Fusion
Pedram (2003)[27]	Subjective unpleasant sensation during swallowing, odynophagia, dysphagia or impaired swallowing during postop: C: 130 (82.3%) S: 56 (71.8%) NS Objective fiber optic ENT exam for pharyngolaryngeal lesions, 24-36 h postop: • Absence of lesion C: 12 (7.59%) S: 32 (41%) $P < .0001$ • Slight C: 63 (39.8%) S: 37 (47.4%) NS • Moderate C: 59 (37.3%) S: 8 (10.2%) $P < .0001$ • Severe C: 22 (13.9%) S: 1 (1.2%) $P < .0001$ • Very severe C: 2 (1.26%) S: 0 (0%) $P < .0001$ Overall: lesions were more frequent in group C, $P < .0001$, RR: 1.57 (CI = 1.3-1.9)	—	Respiratory distress C: 2 (both had a revision surgery for drainage of cervical hematoma) S: 0	—	C: 88 (55%), 66 (41.7%) local nebulization of a corticosteroid, 22 (13.9%) methylprednisolone IV S: 0 $P < .0001$	—	—
Emery (2009)[28]	—	—	Delayed extubation (>1 day) C: 6 (19.3%) S: 5 (14.2%) NS, $P = .22$	C: 4.645 d S: 4.371 d NS, $P = .47$	—	—	—
Lee (2011)[16]	VAS (odynophagia) • Immediately postop C: 5.3 S: 2.5 $P = .000$ • 4 d postop C: 4.6 S: 1.5 $P = .000$ • 2 w postop C: 3.5 S: 1.2 $P = .000$	PSTSI in C3-C5 on RG • Immediately postop C: 74.3% S: 58.2% $P = .004$ • 2 d postop C: 84.1% S: 57.9% $P = .000$ • 4 d postop C: 82.9% S: 56.3% $P = .000$ • 2 w postop C: 51.4% S: 44.9% $P = .036$	—	—	—	—	With RG and CT scan at last FU C: 24 (96%) S: 25 (100%)

(continued)

Table 2. (continued)

Author, Year	Dysphagia/Odynophagia	Prevertebral Soft Tissue Swelling	Airway Compromise	Length of Hospital Stay	Postoperative Steroid Need	Steroid-Related Complications	Fusion
Nam (2013)[29]	VAS (odynophagia) • Immediately postop C: 1.9 ± 0.8 S1: 1.9 ± 0.9 S2: 1.9 ± 0.7 NS, $P = .970$ • 1 d postop C: 3.0 ± 0.8 S1: 2.9 ± 1.0 S2: 3.0 ± 0.8 NS, $P = .810$ • 2 d postop C: 2.5 ± 1.0 S1: 2.5 ± 0.9 S2: 2.6 ± 1.1 NS, $P = .936$ • 3 d postop C: 2.0 ± 1.1 S1: 1.8 ± 0.9 S2: 2.0 ± 0.9 NS, $P = .792$ • 4 d postop C: 1.4 ± 1.0 S1: 1.2 ± 0.7 S2: 1.5 ± 0.7 NS, $P = .353$ • 5 d postop C: 1.0 ± 1.0 S1: 0.6 ± 0.6 S2: 1.0 ± 0.6 NS, $P = .078$	PSTD in C1-C7 on RG • Immediately postop C: 1629 ± 229 cm^2 S1: 1533 ± 224 cm^2 S2: 1520 ± 226 cm^2 NS, $P = .237$ • 1 d postop C: 1789 ± 267 cm^2 S1: 1699 ± 258 cm^2 S2: 1689 ± 248 cm^2 NS, $P = .387$ • 2 d postop C: 1963 ± 338 cm^2 S1: 1865 ± 318 cm^2 S2: 1836 ± 321 cm^2 NS, $P = .419$ • 3 d postop C: 1966 ± 302 cm^2 S1: 1886 ± 282 cm^2 S2: 1867 ± 282 cm^2 NS, $P = .501$ • 4 d postop C: 1853 ± 301 cm^2 S1: 1776 ± 307 cm^2 S2: 1747 ± 251 cm^2 NS, $P = .473$ • 5 d postop C: 1706 ± 335 cm^2 S1: 1576 ± 292 cm^2 S2: 1541 ± 305 cm^2 NS, $P = .202$	VAS (dyspnea) • Immediately postop C: 1.4 ± 0.7 S1: 1.0 ± 0.6 S2: 0.9 ± 0.6 $P = .018$ • 1 d postop C: 2.4 ± 0.8 S1: 1.8 ± 0.7 S2: 1.9 ± 0.7 $P = .043$ • 2 d postop C: 2.5 ± 0.9 S1: 2.0 ± 0.8 S2: 1.9 ± 0.7 $P = .027$ • 3 d postop C: 1.6 ± 0.7 S1: 1.8 ± 0.7 S2: 1.8 ± 0.6 NS, $P = .695$ • 4 d postop C: 1.1 ± 0.8 S1: 1.0 ± 0.9 S2: 1.0 ± 0.7 NS, $P = .833$ • 5 d postop C: 0.6 ± 0.7 S1: 0.6 ± 0.7 S2: 0.5 ± 0.6 NS, $P = .653$	—	—	—	—
Song (2014)[30]	Dysphagia with Bazaz scale • 1 d postop C: 20 (100%) svr S: 19 (95%) svr, 1 (5%) mod NS, $P = .311$ • 2 d postop C: 14 (70%) svr, 6 (30%) mod S: 7 (35%) svr, 13 (65%) mod $P = .027$ • 3 d postop C: 8 (40%) svr, 12 (60%) mod S: 4 (20%) svr, 11 (55%) mod, 5 (25%) mld $P = .041$ • 4 d postop C: 4 (20%) svr, 13 (65%) mod, 3 (15%) mld S: 8 (40%) mod, 12 (60%) mld $P = .005$ • 5 d postop C: 14 (70%) mod, 6 (30%) mld S: 4 (20%) mod, 14 (70%) mld, 2 (10%) none $P = .005$	PSTS summation of C2-C7 on RG • 1 d postop C: 95.5 ± 18.1 mm S: 84.7 ± 17.1 mm NS, $P = .61$ • 2 d postop C: 103.5 ± 19.2 mm S: 82.2 ± 14.6 mm $P < .001$ • 3 d postop C: 103.9 ± 21.8 mm S: 79.4 ± 12.7 mm $P < .001$ • 4 d postop C: 108.9 ± 14.6 mm S: 76.5 ± 12.7 mm $P < .001$ • 5 d postop C: 105 ± 14.3 mm S: 78.2 ± 13.9 mm $P < .001$	—	C: 6.0 ± 1.02 d (range 4-7) S: 5.1 ± 0.7 d (range 4-7) $P = .003$	—	None	—

(continued)

Table 2. (continued)

Author, Year	Dysphagia/Odynophagia	Prevertebral Soft Tissue Swelling	Airway Compromise	Length of Hospital Stay	Postoperative Steroid Need	Steroid-Related Complications	Fusion
		• 6 d postop C: 107.8 ± 17.0 mm S: 65.4 ± 3.6 mm $P < .001$ • 7 d postop C: 100.0 ± 19.0 mm S: 73.5 ± 8.7 mm NS, $P = .091$					
Jeyamohan (2015)[31]	FOSS • 1 m postop C: 0.66 S: 0.064 $P = .027$ • 3 m postop C: 0.261 S: 0.14 NS, $P = .445$ • 6 m postop C: 0.174 S: 0.2 NS, $P = .768$ • 12 m postop C: 0.1 S: 0.26 NS, $P = .375$ • 24 m postop C: 0.041 S: 0.115 NS, $P = .333$	—	Airway compromise rate: 2.7%	—	C: 8 (14.3%) S: 1 (1.8%)	—	CT scan • 6 m postop C: 60% S: 39.5% $P = .047$ • 12 m postop C: 80% S: 75% NS, $P = .57$ • 24 m postop C: 95.2% S: 92.7% NS, $P = .572$
Edwards (2016)[32]	Number of patients *without* dysphagia • 1 d postop C: 7 (30.4%) S: 4 (14.8%) NS, $P = .305$ • 4 d postop C: 3 (13.0%) S: 16 (59.3%) $P = .001$ • 7 d postop C: 5 (21.7%) S: 16 (59.3%) $P = .010$ • 14 d postop C: 7 (30.4%) S: 18 (66.7%) $P = .022$ • 28 d postop C: 6 (26.1%) S: 15 (55.6%) $P = .047$ Dysphagia with modified Bazaz scale • 1 d postop C: 1.09 ± 0.900 S: 1.04 ± 0.649 NS, $P = .839$	—	Adverse airway events: C: 1 (4.3%), readmission for breathing difficulty S: 0 NS, $P = .460$	C: 24.42 h S: 24.97 h NS, $P = .612$	C: 4 (17.4%) S: 1 (3.7%) NS, $P = .167$	None	—

(continued)

Table 2. (continued)

Author, Year	Dysphagia/Odynophagia	Prevertebral Soft Tissue Swelling	Airway Compromise	Length of Hospital Stay	Postoperative Steroid Need	Steroid-Related Complications	Fusion
	• 4 d postop C: 1.74 ± 1.05 S: 0.52 ± 0.700 *P* < .001 • 7 d postop C: 1.43 ± 1.04 S: 0.56 ± 0.751 *P* < .002 • 14 d postop C: 1.39 ± 1.20 S: 0.52 ± 0.802 *P* = .005 • 28 d postop C: 1.35 ± 1.11 S: 0.59 ± 0.747 *P* = .012						
Cancienne (2016)[33]	Incidence of dysphagia after 1-2 level ACDF within 90 days postop C: 16,582 (8.4%) S: 133 (7.5%) NS, *P* = .198 Incidence of dysphagia after ≥3-level ACDF within 90 days postop C: 6631 (14.6%) S: 29 (9.0%) *P* = .005	—	—	For 1-2 level ACDF within 90 days postop C: 2 ± 2.2 d S: 1 ± 1.1 d *P* < .0001 For ≥3-level ACDF within 90 days postop C: 3 ± 2.8 d S: 2 ± 1.3 d *P* < .0001	—	Combined rates of infection and wound breakdown within 90 days postop C: 1.6% S: 1.7% NS, *P* = .717, OR: 0.9 (CI = 0.7-1.3)	—
Koreckij (2016)[34]	Dysphagia with Bazaz scale • 6 w postop C: 40.9% svr, 27.3% mod, 9.1% mld, 22.7% none S: 14.3% svr, 14.3% mod, 9.5% mld, 61.9% none *P* = .008 • 3 m postop C: 23.8% svr, 19% mod, 9.5% mld, 47.6% none S: 9.5% mod, 14.3% mld, 76.2% none *P* = .022 Dysphagia with EAT-10 • 6w postop C: 28.6% nl S: 59.1% nl NS, *P* = .067 • 3 m postop C: 42.9% nl S: 81.8% nl *P* = .012	PSTSI in C3-C7 on RG • 1 d postop C: 1.19 ± 0.24 S: 1.33 ± 0.26 NS, *P* = .09 • 6 w postop C: 1.58 ± 0.70 S: 1.62 ± 0.36 2NS, *P* = .93	—	C: 2.2 ± 1.9 d S: 1.27 ± 0.6 d *P* = .03	—	—	—

Abbreviations: C, control/sham/placebo group; CI, confidence interval; CT, computed tomography; d, day(s); FOSS, Functional Outcome Swallowing Scale; FU, follow-up; h, hour(s); JOA, Japanese Orthopaedic Association; mld, mild; mod, moderate; m, month; NDI, Neck Disability Index; nl, normal; NS, nonsignificant; OR, odds ratio; PSTD, prevertebral soft tissue density; PSTSI, prevertebral soft tissue swelling index; RF, retropharyngeal; RG, radiography; RR, relative risk; S, steroid group; SF-12, 12-Item Short-Form Health Survey; svr, severe; VAS, Visual Analogue Scale, w, week(s).

steroid group during the first 2 days postoperative. However, there was no significant difference within the third to the fifth days postoperative.

Length of Hospital Stay

Both RCTs reporting hospitalization period found no difference between the steroid and control groups.[28,32] In contrast, both nonrandomized studies proved a significantly shorter hospital stay with steroid treatment.[33,34]

Postoperative Steroid Need

This outcome was defined as the proportion of patients who required treatment with corticosteroids in the control group or required extra doses of steroid, additional to the main protocol, in the steroid group. Three studies reported this outcome to be higher in the control group compared with the steroid group, as follows: Pedram et al[27] (55% vs 0%, $P < .0001$), Jeyamohan et al[31] (14.3% vs 1.8%), and Edwards et al[32] (17.4% vs 3.7%, $P > .05$).

Steroid-Related Complications

Song et al[30] followed the patients for 3 months for complications such as peptic ulcer disease or operation site infections and reported no complications. Likewise, Edwards et al[32] found no infection, delayed healing, or diabetes. Combined rates of infection and wound breakdown were measured by Cancienne et al[33] within 90 days postoperative. There was no significant difference between the control and steroid groups (1.6% vs 1.7%, respectively).

Fusion

Only 2 studies reported fusion rate. Lee et al[16] observed complete fusion at the latest follow-up (range 16-32 months) in the lateral radiographs and computed tomography scans of the patients treated with steroid, while they found one nonunion in the control group. Jeyamohan et al[31] performed computed tomography scans at 6, 12, and 24 months postoperation. The fusion rate was significantly lower in the steroid group compared with the control at the 6-month follow-up (39.5% vs 60%, respectively), whereas this difference disappeared at subsequent follow-ups (at 24 months, 92.7% vs 95.2%, respectively).

Discussion

In this study, we reviewed the current evidence of steroid use in anterior cervical spine surgery. Seven RCTs, one case-control study, and one cohort study were included. The risk of bias assessment showed that the quality of studies was generally low, since both the nonrandomized studies were retrograde and only 2 out of 7 randomized studies had acceptable method of randomization.

Dysphagia significantly decreased with corticosteroids. This finding was confirmed by all studies except the one performed by Nam et al,[29] in which they reported no significant difference between the control and 2 steroid groups with different doses. This may be due to their limited inclusion criteria that only recruited patients with 1-level ACDF and excluded the procedures on 2 or more levels. Cancienne et al[33] found significant effects of steroids only in ACDF $\geq$3 levels; in contrast, Lee et al[16] showed that dysphagia was significantly lowered by steroids in 1- or 2-level ACDF. Despite some controversies, all studies proved steroids to be beneficial in prevention of dysphagia after anterior cervical procedures for more than 2 levels of fusion. This discrepancy implies the importance of steroid trials comparing the outcomes between single- and multilevel procedures. Furthermore, since there is no sufficient evidence on validity of most of the measures of dysphagia that were used in these studies, their findings must be interpreted with caution.

PSTS and airway compromise were reported in less than 50% of studies. PSTS was generally in accordance with findings of dysphagia. Airway compromise is not a common complication and was only reported in 3 studies. There was a vast variation in assessment methods and the results. Surprisingly, although Nam et al[29] determined no significant effect of steroids on reduction of dysphagia and PSTS, they reported a significantly lower VAS score for dyspnea in steroid group. The other 2 studies found no significant difference between the steroid group and controls in their assessments for airway compromise.[28,32]

Two major concerns regarding the use of corticosteroids are steroid-related complications and reduced/delayed fusion. In those few studies that addressed these outcomes, no complications or long-term reduction of fusion rates were reported. However, as reported by Jeyamohan et al,[31] the fusion rate was significantly delayed in the steroid group at the 6-month follow-up. As the current evidence is not enough, it is necessary to appraise the effect of steroids on fusion rate in the forthcoming studies with long-term designs.

The form, dose, and type of corticosteroid drug, as well as the methods of outcome evaluation were different in the included studies. This heterogeneity made the data pooling and meta-analysis impossible. Further clinical trials with appropriate design and sample size are needed to reach a definite conclusion.

Conclusion

Current literature consistently supports the use of steroids for prevention of complication such as dysphagia in patients undergoing anterior cervical spine surgery with fusion. However, these findings are limited by poor methodological quality of the studies, particularly by the indeterminate quality of the outcome measurement instruments. Furthermore, lack of comparisons between single- and multilevel surgeries and limited number of steroid trials that evaluate the fusion rate, airway compromise, and PSTS are the areas of concern that are recommended to be addressed in future studies.

Appendix

Search Strategy

PubMed. (Anterior) AND ("Cervical Vertebrae"[Mesh] OR "Neck"[Mesh] OR cervical OR neck) AND ("Diskectomy"[Mesh] OR "Decompression, Surgical"[Mesh] OR "Intervertebral Disc"[Mesh] OR "Intervertebral Disc Degeneration"[Mesh] OR "Intervertebral Disc Displacement"[Mesh] OR "Discitis"[Mesh] OR "Radiculopathy"[Mesh] OR "Spinal Cord Diseases"[Mesh] OR discectomy OR diskectomy OR decompression OR corpectomy OR radiculopath* OR myelopath* OR radiculomyelopath* OR radiculo-myelopath* OR myeloradiculopath* OR myelo-radiculopath* OR diskitis OR discitis OR discopath* OR ((disc* OR disk*) AND (degenerat* OR displace* OR hernia*)) OR "Spinal Fusion"[Mesh] OR "Arthrodesis"[Mesh] OR fusion OR arthrodesis) AND ("Glucocorticoids"[Mesh] OR "Adrenal Cortex Hormones"[Mesh] OR "Steroids"[Mesh] OR "Dexamethasone"[Mesh] OR "Betamethasone"[Mesh] OR "Hydrocortisone"[Mesh] OR "Cortisone"[Mesh] OR "Prednisolone"[Mesh] OR "Methylprednisolone"[Mesh] OR "Methylprednisolone Hemisuccinate"[Mesh] OR "Triamcinolone"[Mesh] OR "Triamcinolone Acetonide"[Mesh] OR "Budesonide"[Mesh] OR "Fludrocortisone"[Mesh] OR "Fluprednisolone"[Mesh] OR "Paramethasone"[Mesh] OR glucocortic* OR gluco-cortic* OR corticosteroid* OR cortico-steroid* OR corticoid* OR steroid* OR corticotropin OR dexamethason* OR dexametason* OR betamethason* OR betametason* OR hydrocortison* OR cortison* OR predniso* OR methylpredniso* OR methyl-predniso* OR triamcinolon* OR budesonid* OR fludrocortison* OR fluprednisolon* OR paramethason*)

Embase

#1. anterior
#2. 'cervical spine'/exp
#3. 'neck'/exp
#4. cervical
#5. neck
#6. 'cervical spine'/exp OR 'neck'/exp OR cervical OR neck
#7. 'intervertebral diskectomy'/exp
#8. 'spinal cord decompression'/exp
#9. 'intervertebral disk'/exp
#10. 'intervertebral disk degeneration'/exp
#11. 'intervertebral disk hernia'/exp
#12. 'radiculopathy'/exp
#13. 'cervical myelopathy'/exp
#14. Discectomy
#15. Diskectomy
#16. Decompression
#17. corpectomy
#18. radiculopath*
#19. myelopath*
#20. radiculomyelopath*
#21. 'radiculo myelopath*'
#22. myeloradiculopath*
#23. 'myelo radiculopath*'
#24. discopath*
#25. 'diskitis'/exp
#26. Diskitis
#27. Discitis
#28. disc* OR disk*
#29. degenerat* OR displace* OR hernia*
#30. disc* OR disk* AND (degenerat* OR displace* OR hernia*)
#31. 'anterior spine fusion'/exp
#32. fusion
#33. Arthrodesis
#34. 'intervertebral diskectomy'/exp OR 'spinal cord decompression'/exp OR 'intervertebral disk'/exp OR 'intervertebral disk degeneration'/exp OR 'intervertebral disk hernia'/exp OR 'radiculopathy'/exp OR 'cervical myelopathy'/exp OR discectomy OR diskectomy OR decompression OR corpectomy OR radiculopath* OR myelopath* OR radiculomyelopath* OR 'radiculo myelopath*' OR myeloradiculopath* OR 'myelo radiculopath*' OR discopath* OR 'diskitis'/exp OR diskitis OR discitis OR (disc* OR disk* AND (degenerat* OR displace* OR hernia*)) OR 'anterior spine fusion'/exp OR fusion OR arthrodesis
#35. 'glucocorticoid'/exp
#36. 'steroid'/exp
#37. 'corticosteroid'/exp
#38. 'dexamethasone'/exp
#39. 'betamethasone'/exp
#40. 'hydrocortisone'/exp
#41. 'cortisone'/exp
#42. 'prednisolone'/exp
#43. 'methylprednisolone'/exp
#44. 'methylprednisolone sodium succinate'/exp
#45. 'triamcinolone'/exp
#46. 'triamcinolone acetonide'/exp
#47. 'budesonide'/exp
#48. 'fludrocortisone'/exp
#49. 'fluprednisolone'/exp
#50. 'paramethasone'/exp
#51. glucocortic*
#52. 'gluco cortic*'
#53. corticosteroid*
#54. 'cortico steroid*'
#55. corticoid*
#56. steroid*
#57. Corticotropin
#58. dexamethason*
#59. dexametason*
#60. betamethason*
#61. betametason*
#62. hydrocortison*
#63. cortison*
#64. predniso*
#65. methylpredniso*
#66. 'methyl predniso*'
#67. triamcinolon*

#68. budesonid*
#69. fludrocortison*
#70. fluprednisolon*
#71. paramethason*
#72. 'glucocorticoid'/exp OR 'steroid'/exp OR 'corticosteroid'/exp OR 'dexamethasone'/exp OR 'betamethasone'/exp OR 'hydrocortisone'/exp OR 'cortisone'/exp OR 'prednisolone'/exp OR 'methylprednisolone'/exp OR 'methylprednisolone sodium succinate'/exp OR 'triamcinolone'/exp OR 'triamcinolone acetonide'/exp OR 'budesonide'/exp OR 'fludrocortisone'/exp OR 'fluprednisolone'/exp OR 'paramethasone'/exp OR glucocortic* OR 'gluco cortic*' OR corticosteroid* OR 'cortico steroid*' OR corticoid* OR steroid* OR corticotropin OR dexamethason* OR dexametason* OR betamethason* OR betametason* OR hydrocortison* OR cortison* OR predniso* OR methylpredniso* OR 'methyl predniso*' OR triamcinolon* OR budesonid* OR fludrocortison* OR fluprednisolon* OR paramethason*
#73. anterior AND ('cervical spine'/exp OR 'neck'/exp OR cervical OR neck) AND ('intervertebral diskectomy'/exp OR 'spinal cord decompression'/exp OR 'intervertebral disk'/exp OR 'intervertebral disk degeneration'/exp OR 'intervertebral disk hernia'/exp OR 'radiculopathy'/exp OR 'cervical myelopathy'/exp OR discectomy OR diskectomy OR decompression OR corpectomy OR radiculopath* OR myelopath* OR radiculomyelopath* OR 'radiculo myelopath*' OR myeloradiculopath* OR 'myelo radiculopath*' OR discopath* OR 'diskitis'/exp OR diskitis OR discitis OR (disc* OR disk* AND (degenerat* OR displace* OR hernia*)) OR 'anterior spine fusion'/exp OR fusion OR arthrodesis) AND ('glucocorticoid'/exp OR 'steroid'/exp OR 'corticosteroid'/exp OR 'dexamethasone'/exp OR 'betamethasone'/exp OR 'hydrocortisone'/exp OR 'cortisone'/exp OR 'prednisolone'/exp OR 'methylprednisolone'/exp OR 'methylprednisolone sodium succinate'/exp OR 'triamcinolone'/exp OR 'triamcinolone acetonide'/exp OR 'budesonide'/exp OR 'fludrocortisone'/exp OR 'fluprednisolone'/exp OR 'paramethasone'/exp OR glucocortic* OR 'gluco cortic*' OR corticosteroid* OR 'cortico steroid*' OR corticoid* OR steroid* OR corticotropin OR dexamethason* OR dexametason* OR betamethason* OR betametason* OR hydrocortison* OR cortison* OR predniso* OR methylpredniso* OR 'methyl predniso*' OR triamcinolon* OR budesonid* OR fludrocortison* OR fluprednisolon* OR paramethason*)

OVID

1. Anterior.mp.
2. Cervical Vertebrae/
3. Neck/
4. cervical.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
5. neck.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
6. 2 or 3 or 4 or 5
7. Diskectomy/
8. Decompression, Surgical/
9. Intervertebral Disc/
10. Intervertebral Disc Degeneration/ or Intervertebral Disc Displacement/
11. Discitis/
12. Radiculopathy/
13. Spinal Cord Diseases/
14. discectomy.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
15. diskectomy.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
16. decompression.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
17. corpectomy.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
18. discitis.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
19. diskitis.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
20. radiculopath*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
21. myelopath*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
22. radiculomyelopath*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
23. radiculo-myelopath*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
24. myeloradiculopath*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

25. myelo-radiculopath*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
26. discopath*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
27. disc*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
28. disk*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
29. degenerat*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
30. displace*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
31. hernia*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
32. Spinal Fusion/
33. Arthrodesis/
34. fusion.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
35. arthrodesis.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
36. 27 or 28
37. 29 or 30 or 31
38. 36 and 37
39. 7 or 8 or 9 or 10 or 12 or 14 or 15 or 16 or 17 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 32 or 33 or 34 or 35 or 38
40. Glucocorticoids/
41. Adrenal Cortex Hormones/
42. Steroids/
43. Dexamethasone/
44. Betamethasone/
45. Hydrocortisone/
46. Cortisone/
47. Prednisolone/
48. Methylprednisolone/
49. Methylprednisolone Hemisuccinate/
50. Triamcinolone/
51. Triamcinolone Acetonide/
52. Budesonide/
53. Fludrocortisone/
54. Fluprednisolone/
55. Paramethasone/
56. glucocortic*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
57. gluco-cortic*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
58. corticosteroid*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
59. cortico-steroid*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
60. corticoid*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
61. steroid*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
62. corticotropin.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
63. dexamethason*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
64. dexametason*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
65. betamethason*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
66. betametason*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
67. hydrocortison*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
68. cortison*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

69. predniso*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
70. methylpredniso*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
71. methyl-predniso*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
72. triamcinolon*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
73. budesonid*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
74. fludrocortison*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
75. fluprednisolon*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
76. paramethason*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
77. 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73 or 74 or 75 or 76
78. 1 and 6 and 39 and 77

Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: Shayan Abdollah Zadegan, Aidin Abedi, Seyed Behnam Jazayeri, Hirbod Nasiri Bonaki, Seyed Behzad Jazayeri, and Vafa Rahimi-Movaghar have no conflicts of interest to disclose. Alexander R. Vaccaro: Replication Medica: Stock/stock option ownership interests; DePuy: Consulting/independent contractor; Medtronics: Consulting/independent contractor, Receipt of royalty payments; Stryker Spine: Consulting/independent contractor, Receipt of royalty payments; Globus: Consulting/independent contractor, Receipt of royalty payments, Stock/stock option ownership interests; Paradigm Spine: Stock/stock option ownership interests; Stout Medical: Consulting/independent contractor, Stock/stock option ownership interests; Progressive Spinal Technologies: Service on scientific advisory board/board of directors/service on committees, Stock/stock option ownership interests; Advanced Spinal Intellectual Properties: Stock/stock option ownership interests; Aesculap: Receipt of royalty payments; Spine Medica: Stock/stock option ownership interests; Computational Biodynamics: Stock/stock option ownership interests; Spinology: Stock/stock option ownership interests; Flagship Surgical: Service on scientific advisory board/board of directors/service on committees, Stock/stock option ownership interests; Cytonics: Stock/stock option ownership interests; Bonovo Orthopaedics: Stock/stock option ownership interests; Electrocore: Stock/stock option ownership interests; Gamma Spine: Stock/stock option ownership interests; Insight Therapeutics: Stock/stock option ownership interests; FlowPharma: Stock/stock option ownership interests; Gerson Lehrman Group: Consulting/independent contractor; Guidepoint Global: Consulting/independent contractor; Medacorp: Consulting/independent contractor; Rothman Institute and Related Properties: Stock/stock option ownership interests; AO Spine: Service on scientific advisory board/board of directors/service on committees; Innovative Surgical Design: Consulting/independent contractor, Service on scientific advisory board/board of directors/service on committees, and Stock/stock option ownership interests; Orthobullets: Consulting/independent contractor; Thieme: Receipt of royalty payments; Jaypee: Receipt of royalty payments; Elsevier: Receipt of royalty payments; Taylor Francis/Hodder and Stoughton: Receipt of royalty payments; Expert testimony: Consulting/independent contractor; Vertiflex: Stock/stock option ownership interests; Avaz Surgical: Stock/stock option ownership interests; *Clinical Spine Surgery*: Deputy editor/editor; *Spine Journal*: Deputy editor/editor; Prime Surgeons: Service on scientific advisory board/board of directors/service on committees; Stock/stock option ownership interests; Dimension Orthotics, LLC: Stock/stock option ownership interests; Spine Therapy Network, Inc: Service on scientific advisory board/board of directors/service on committees; Vexim: Consulting/independent contractor, Receipt of royalty payments; SpineWave: Consulting/independent contractor, Receipt of royalty payments.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This study was supported by AOSpine of Middle East (AOSME) and Sina Trauma and Surgery Research Center, Tehran University of Medical Sciences (Tehran, Iran).

References

1. Smith GW, Robinson RA. The treatment of certain cervical-spine disorders by anterior removal of the intervertebral disc and interbody fusion. *J Bone Joint Surg Am*. 1958;40:607-624.
2. Emery SE.Anterior approaches for cervical spondylotic myelopathy: Which? When? How? *Eur Spine J*. 2015;24(suppl 2): 150-159.
3. Campbell PG, Yadla S, Malone J, et al. Early complications related to approach in cervical spine surgery: single-center prospective study. *World Neurosurg*. 2010;74:363-368.
4. Feng YT, Hwang SL, Lin CL, Lee IC, Lee KT. Safety and resource utilization of anterior cervical discectomy and fusion. *Kaohsiung J Med Sci*. 2012;28:495-499.
5. Sagi HC, Beutler W, Carroll E, Connolly PJ. Airway complications associated with surgery on the anterior cervical spine. *Spine (Phila Pa 1976)*. 2002;27:949-953.
6. Daniels AH, Riew KD, Yoo JU, et al. Adverse events associated with anterior cervical spine surgery. *J Am Acad Orthop Surg*. 2008;16:729-738.

7. Anderson KK, Arnold PM. Oropharyngeal dysphagia after anterior cervical spine surgery: a review. *Global Spine J*. 2013;3: 273-286.
8. Bazaz R, Lee MJ, Yoo JU. Incidence of dysphagia after anterior cervical spine surgery: a prospective study. *Spine (Phila Pa 1976)*. 2002;27:2453-2458.
9. Smith-Hammond CA, New KC, Pietrobon R, Curtis DJ, Scharver CH, Turner DA. Prospective analysis of incidence and risk factors of dysphagia in spine surgery patients: comparison of anterior cervical, posterior cervical, and lumbar procedures. *Spine (Phila Pa 1976)*. 2004;29:1441-1446.
10. Khaki F, Zusman NL, Nemecek AN, Ching AC, Hart RA, Yoo JU. Postoperative prevertebral soft tissue swelling does not affect the development of chronic dysphagia following anterior cervical spine surgery. *Spine (Phila Pa 1976)*. 2013;38: E528-E532.
11. Boockvar JA, Philips MF, Telfeian AE, O'Rourke DM, Marcotte PJ. Results and risk factors for anterior cervicothoracic junction surgery. *J Neurosurg*. 2001;94(1 suppl):S12-S17.
12. Emery SE, Smith MD, Bohlman HH. Upper-airway obstruction after multilevel cervical corpectomy for myelopathy. *J Bone Joint Surg Am*. 1991;73:544-551.
13. Krnacik MJ, Heggeness MH. Severe angioedema causing airway obstruction after anterior cervical surgery. *Spine (Phila Pa 1976)*. 1997;22:2188-2190.
14. Penberthy A, Roberts N. Recurrent acute upper airway obstruction after anterior cervical fusion. *Anaesth Intensive Care*. 1998; 26:305-307.
15. Riew KD, Sethi NS, Devney J, Goette K, Choi K. Complications of buttress plate stabilization of cervical corpectomy. *Spine (Phila Pa 1976)*. 1999;24:2404-2410.
16. Lee SH, Kim KT, Suk KS, Park KJ, Oh KI. Effect of retropharyngeal steroid on prevertebral soft tissue swelling following anterior cervical discectomy and fusion: a prospective, randomized study. *Spine (Phila Pa 1976)*. 2011;36:2286-2292.
17. Lim S, Kesavabhotla K, Cybulski GR, Dahdaleh NS, Smith ZA. Predictors for airway complications following single- and multilevel anterior cervical discectomy and fusion. *Spine (Phila Pa 1976)*. 2017;42:379-384.
18. Higgins JPT, Green S. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0. The Cochrane Collaboration. http://handbook.cochrane.org/. Published 2011. Accessed April 28, 2017.
19. Furlan AD, Malmivaara A, Chou R, et al. 2015 updated method guideline for systematic reviews in the Cochrane Back and Neck Group. *Spine (Phila Pa 1976)*. 2015;40:1660-1673.
20. Furlan AD, Pennick V, Bombardier C, van Tulder M. 2009 updated method guidelines for systematic reviews in the Cochrane Back Review Group. *Spine (Phila Pa 1976)*. 2009;34: 1929-1941.
21. Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. *BMJ*. 2009;339:b2700. doi:10.1136/bmj.b2700.
22. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med*. 2009;6:e1000097.
23. Moher D, Shamseer L, Clarke M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Syst Rev*. 2015;4:1. doi:10.1186/2046-4053-4-1.
24. Slim K, Nini E, Forestier D, Kwiatkowski F, Panis Y, Chipponi J. Methodological index for non-randomized studies (MINORS): development and validation of a new instrument. *ANZ J Surg*. 2003;73:712-716.
25. Zeng X, Zhang Y, Kwong JS, et al. The methodological quality assessment tools for preclinical and clinical studies, systematic review and meta-analysis, and clinical practice guideline: a systematic review. *J Evid Based Med*. 2015;8:2-10. doi:10.1111/jebm.12141.
26. Kim SY, Park JE, Lee YJ, et al. Testing a tool for assessing the risk of bias for nonrandomized studies showed moderate reliability and promising validity. *J Clin Epidemiol*. 2013;66:408-414.
27. Pedram M, Castagnera L, Carat X, Macouillard G, Vital JM. Pharyngolaryngeal lesions in patients undergoing cervical spine surgery through the anterior approach: contribution of methylprednisolone. *Eur Spine J*. 2003;12:84-90.
28. Emery SE, Akhavan S, Miller P, et al. Steroids and risk factors for airway compromise in multilevel cervical corpectomy patients: a prospective, randomized, double-blind study. *Spine (Phila Pa 1976)*. 2009;34:229-232. doi:10.1097/BRS.0b013e318193a287.
29. Nam TW, Lee DH, Shin JK, Goh TS, Lee JS. Effect of intravenous dexamethasone on prevertebral soft tissue swelling after anterior cervical discectomy and fusion. *Acta Orthop Belg*. 2013;79:211-215.
30. Song KJ, Lee SK, Ko JH, Yoo MJ, Kim DY, Lee KB. The clinical efficacy of short-term steroid treatment in multilevel anterior cervical arthrodesis. *Spine J*. 2014;14:2954-2958.
31. Jeyamohan SB, Kenning TJ, Petronis KA, Feustel PJ, Drazin D, DiRisio DJ. Effect of steroid use in anterior cervical discectomy and fusion: a randomized controlled trial. *J Neurosurg Spine*. 2015;23:137-143.
32. Edwards CC, Dean C, Phillips D, Blight A. Can dysphagia following anterior cervical fusions with rhBMP-2 be reduced with local depomedrol application? A prospective, randomized, placebo-controlled, double-blind trial. *Spine (Phila Pa 1976)*. 2016;41:555-562.
33. Cancienne JM, Werner BC, Loeb AE, et al. The effect of local intraoperative steroid administration on the rate of postoperative dysphagia following ACDF: a study of 245,754 patients. *Spine (Phila Pa 1976)*. 2016;41:1084-1088.
34. Koreckij TD, Davidson AA, Baker KC, Park DK. Retropharyngeal steroids and dysphagia following multilevel anterior cervical surgery. *Spine (Phila Pa 1976)*. 2016;41:E530-E534.
35. Krol R, Jach K, Zietek P. Dysphagia in the course of degenerative changes of the anterior wall of the cervical spine [in Polish]. *Chir Narzadow Ruchu Ortop Pol*. 1999;64:251-255.
36. Kumar VR, Tripathy DK, Sivashanmugam T, Ravishankar M. Bilateral vocal cord edema following anterior cervical discectomy-usefulness of bonfils retromolar fiberscope. *Anesth Essays Res*. 2014;8:413-415.
37. Lee SH, Mesfin A, Riew KD. Delayed esophageal perforation after anterior cervical fusion and retropharyngeal steroid use: a report of two cases. *Spine J*. 2015;15:e75-e80.

38. Perri B, Cooper M, Lauryssen C, Anand N. Adverse swelling associated with use of rh-BMP-2 in anterior cervical discectomy and fusion: a case study. *Spine J*. 2007;7:235-239.
39. Sugar O. Spinal cord malfunction after anterior cervical discectomy. *Surg Neurol*. 1981;15:4-8.
40. Boakye M, Mummaneni PV, Garrett M, Rodts G, Haid R. Anterior cervical discectomy and fusion involving a polyetheretherketone spacer and bone morphogenetic protein. *J Neurosurg. Spine*. 2005;2:521-525.
41. Buttermann GR. Prospective nonrandomized comparison of an allograft with bone morphogenic protein versus an iliac-crest autograft in anterior cervical discectomy and fusion. *Spine J*. 2008;8:426-435.
42. Kukreja S, Ahmed OI, Haydel J, Nanda A, Sin AH. Complications of anterior cervical fusion using a low-dose recombinant human bone morphogenetic protein-2. *Korean J Spine*. 2015;12: 68-74.
43. Lu DC, Tumialan LM, Chou D. Multilevel anterior cervical discectomy and fusion with and without rhBMP-2: a comparison of dysphagia rates and outcomes in 150 patients. *J Neurosurg Spine*. 2013;18:43-49.
44. Stachniak JB, Diebner JD, Brunk ES, Speed SM. Analysis of prevertebral soft-tissue swelling and dysphagia in multilevel anterior cervical discectomy and fusion with recombinant human bone morphogenetic protein-2 in patients at risk for pseudarthrosis. *J Neurosurg Spine*. 2011;14:244-249.
45. Tumialan LM, Pan J, Rodts GE, Mummaneni PV. The safety and efficacy of anterior cervical discectomy and fusion with polyetheretherketone spacer and recombinant human bone morphogenetic protein-2: a review of 200 patients. *J Neurosurg Spine*. 2008;8:529-535.
46. Jeyamohan S, Kenning TJ, Feustel P, Petronis K, Dirisio DJ. Dexamethasone's effect in multiple-level anterior cervical discectomy and fusion. *Clin Neurosurg*. 2013;60: 172-173.
47. Tiebel N, Pilgram-Pastor S, De Kruijf D, Felgenhauer H, Boldt-Gäth A, Buhl R. Determinants for prevertebral soft tissue swelling (PVSTS) after anterior cervical fusion (ACF): interim report of the prospective "prevestis"-study. *Eur Spine J*. 2014;23:2506-2507.
48. Weinstein J, Schroeder JE, Sama AA, Girardi FP. Effect of steroid placement on a gelatin sponge and soft tissue swelling following anterior cervical discectomy and fusion: a radiological analysis. *Spine J*. 2014;14:S116.
49. Joaquim AF, Murar J, Savage JW, Patel AA. Dysphagia after anterior cervical spine surgery: a systematic review of potential preventative measures. *Spine J*. 2014;14:2246-2260.
50. Siasios I, Fountas K, Dimopoulos V, Pollina J. The role of steroid administration in the management of dysphagia in anterior cervical procedures [published online May 27, 2016]. *Neurosurg Rev*. doi:10.1007/s10143-016-0741-8.
51. Epstein NE. Commentary on the effect of steroid use in anterior cervical discectomy and fusion surgery: a randomized controlled trial by Shiveindra B, et al. *Journal of Neurosurgery Spine* 2015; 23:137-43. *Surg Neurol Int*. 2015;6(suppl 19):S508-S511.
52. Ross DA. Letter to the editor: steroid use in anterior cervical discectomy and fusion. *J Neurosurg Spine*. 2016;24:998-1000.
53. Khajavi K, Shen A. Safety and efficacy of bioabsorbable cervical spacers and low-dose rhBMP-2 in multi-level ACDF. *Int J Spine Surg*. 2014;8. doi:10.14444/1009.
54. von der Hoeh NH, Voelker A, Jarvers JS, Gulow J, Heyde CE. Results after the surgical treatment of anterior cervical hyperostosis causing dysphagia. *Eur Spine J*. 2015;24(suppl 4):S489-S493.
55. Wu B, Song F, Zhu S. Reasons of dysphagia after operation of anterior cervical decompression and fusion [published online June 20, 2016]. *Clin Spine Surg*. doi:10.1097/BSD.0000000000000180.
56. Skeppholm M, Ingebro C, Engstrom T, Olerud C. The Dysphagia Short Questionnaire: an instrument for evaluation of dysphagia: a validation study with 12 months' follow-up after anterior cervical spine surgery. *Spine (Phila Pa 1976)*. 2012;37:996-1002.
57. Belafsky PC, Mouadeb DA, Rees CJ, et al. Validity and reliability of the Eating Assessment Tool (EAT-10). *Ann Otol Rhinol Laryngol*. 2008;117:919-924.
58. Salassa JR. A functional outcome swallowing scale for staging oropharyngeal dysphagia. *Dig Dis*. 1999;17:230-234.