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REVIEW

The effect of local intraoperative corticosteroid application on postoperative dysphagia following anterior cervical spine surgery

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Abstract

Dysphagia is a common complication following anterior cervical spine surgery (ACSS). Although several literatures have reported the potential benefit of local corticosteroid application on dysphagia, its safety and efficacy are still unclear. A systematic review was performed aiming to evaluate the evidence of local corticosteroid application in prevention or treatment of postoperative dysphagia following ACSS. A systematic search was performed in September 2018 in PubMed and Embase database. The following information was extracted: study investigator, year of publication, number of patients, study design, inclusion/exclusion criteria, administration protocol of steroid, type of surgical procedure, number of levels performed, assessment methodology of dysphagia, radiologic assessment of prevertebral soft tissue swelling (PSTS), follow-up time points, outcome of dysphagia, and corticosteroid-related complications. Qualitative synthesis was performed. Finally, 5 studies met the inclusion/exclusion criteria. Four studies found that local corticosteroid application could decrease the incidence and magnitude of postoperative dysphagia while 1 study showed no effect on dysphagia significantly at 6 weeks and 3 months follow-up time. A total of 2325 patients received local corticosteroid intraoperatively; no early corticosteroid-related complication was reported. Totally, 4 adverse events occurred in long-term follow-up time, including 2 bone nonunion at 1.5 and 2.5 years postoperatively, 2 esophageal perforation at 2 months and 11 months of follow-up, respectively. Local corticosteroid application can reduce the incidence and severity of dysphagia following ACSS without increasing early corticosteroid-related complications. But further high-quality study is necessary to analyze potential delayed complications.

Keywords Corticosteroid · Anterior cervical spine surgery · Dysphagia · Systematic review

Dysphagia is one of the most common complications associated with anterior cervical spine surgery (ACSS), especially in early period. The reported prevalence ranged from 1 from 73% [1–5]. The causes can be attributed to local soft tissue swelling, retraction of midline structure, recurrent laryngeal nerve palsy, prevertebral hematoma, etc. Of which, local soft tissue swelling is mainly the common cause of dysphagia [1]. It was thought that administration of corticosteroid could alleviate soft tissue swelling and subsequently reduce the incidence of postoperative dysphagia. However, the effect of systemic application of corticosteroid on dysphagia following ACSS is controversial [6–8]. Recently, several literatures have reported the potential benefit of local use of corticosteroid in the prevention of dysphagia. Here, we performed a systematic review aiming to evaluate the evidence of local corticosteroid application in treatment of postoperative dysphagia following ACSS.

Methods

Information sources and search strategy

A comprehensive search of PubMed and Embase databases was performed according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analysis) guidelines in September 10, 2018. Detailed search strategy was provided in the Appendix. Following comprehensive search, the abstracts of these studies were screened for

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relevance. The full text of these articles, which met the following study selection criteria, was reviewed. The reference lists of all selected articles were also manually and thoroughly searched. The initial study screen and review was conducted by two independent reviewers. Disagreements were solved by discussion, in which one another author participated.

Study selection

Only studies that evaluated the effect of local corticosteroid application on dysphagia following ACSS due to degenerative pathology, cohort, and randomized control study design, and only English-language studies were enrolled. Exclusion criteria included studies that investigated solely systemic application of steroid in treatment of dysphagia, cervical vertebrae disease other than degenerative pathology, such as tumors, rheumatoid arthritis, and trauma.

Data extraction and synthesis

Data extracted included study investigators, year of publication, number of patients, study design, inclusion/exclusion criteria, administration protocol of steroid, type of surgical procedure, number of levels performed, assessment methodology of dysphagia, radiologic assessment of prevertebral soft tissue swelling (PSTS), follow-up time points, outcome of dysphagia, and corticosteroid-related complications. A meta-analysis and quantitative synthesis were not performed due to the large heterogeneity among those studies. Therefore, we conducted a qualitative synthesis to bring together the key components of studies included.

Results

A total of 1436 articles were obtained from a systematic search in PubMed and Embase databases. After removal of duplicates, 1238 citations were identified. Fourteen potentially relevant articles were selected through title/abstract screening, of which 5 studies finally met our inclusion/ exclusion criteria (Fig. 1). Of the total, 3 articles described prospective randomized controlled trials, and 2 retrospective cohort studies. One study by Jenkins et al. [9] compared the effect of local steroid application with systemic administration of steroid and control group, only the data of local steroid application group and control group was extracted. The paper by Edwards et al. [10] evaluated the efficacy of local depomedrol application in reducing the incidence and severity of postoperative dysphagia following ACSS with bone morphogenetic protein-2 (BMP-2). Details were provided in Tables 1 and 2.

Effect of local corticosteroid application on dysphagia

Of the 5 studies, Edwards et al. [10], Koreckij et al. [12], Cancienne et al. [13], and Jenkins et al. [9] found local intraoperative corticosteroid application significantly reduced the incidence and magnitude of dysphagia. One randomized control trial by Haws et al. [11] showed local depomedrol administration did not improve patient-reported swallowing function or swelling following anterior cervical discectomy and fusion (ACDF) at follow-up 6 weeks and 3 months (see also Table 1). Of note, postoperative dysphagia often occurred in the early postoperative period, the incidence and severity of dysphagia presented a decline trend in the following course [14, 15], and of the 5 studies, Edwards et al. [10], and Jenkins et al. [9] reported the results of early dysphagia treated by local corticosteroid and found local corticosteroid application could improve early dysphagia. More detailed outcomes of postoperative dysphagia were listed in Table 3.

Effect of local corticosteroid application on prevertebral soft tissue swelling

Prevertebral soft tissue swelling (PSTS) is one of the most common contributors to postoperative dysphagia [1]. Corticosteroid can alleviate soft tissue swelling caused by various pathology, thus it was considered that local corticosteroid application may improve postoperative swallowing function. In two studies where postoperative PSTS were assessed, Koreckij et al. [12] found local corticosteroid application tempered PSTS, while Haws et al. [11] showed local administration of corticosteroid had no impact on postoperative PSTS as compared with control group and depomedrol showed no significant effect on swallowing function in patients undergoing either single-level or multiple level ACDF.

Adverse events associated with local corticosteroid application

A total of 246,052 patients were enrolled in the 5 studies, of which 2325 patients received local corticosteroid treatment. Cancienne et al. [13] reported 12 out of 2092 patients who were given local corticosteroid suffered from postoperative wound infection or wound breakdown ,but no significant difference was found as compared with control group (OR 0.9, 95% CI 0.7–1.3, $p = 0.717$). Edwards et al. [10], Koreckij et al. [12], and Haws et al. [11] did not report occurrence of corticosteroid-related complications, such as wound infection, delayed wound healing, wound breakdown, and retropharyngeal abscess. The study by Jenkins et al. [9] showed bone nonunion was confirmed in 2 patients at 1.5 years and 2 years postoperatively, respectively, but no early corticosteroid-related complication was reported.

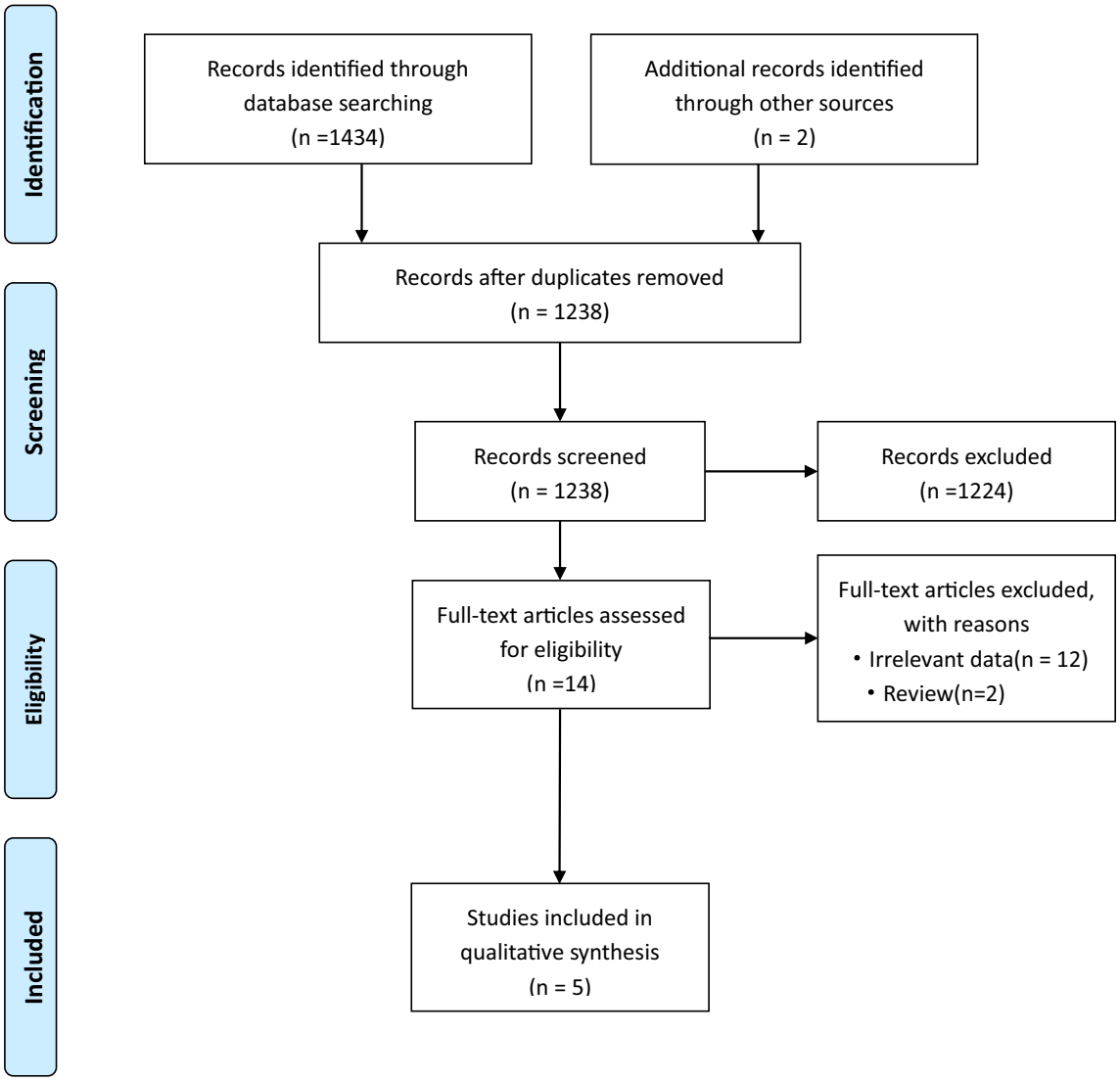

Fig. 1 PRISMA flow diagram

Discussion

Efficacy of local corticosteroid application on dysphagia following ACSS

The result of this systematic review shows a tendency towards supporting local corticosteroid application following ACSS to alleviate dysphagia occurred in the early postoperative period. Of the 5 studies, one RCT study by Haws et al. [11] did not find significant difference in swallowing disorder questionnaire score between local steroid group and control group, but the follow-up time point in that study was scheduled at 6 weeks and 12 weeks postoperatively; outcome of dysphagia in early postoperative period had not been reported. Dysphagia most commonly occurred in early postoperative period; Papavero et al. [16] reported 49.3% of patients complained about dysphagia during 5 days postoperatively. Tervonen et al. [5] found 69% of patients presented dysphagia during 7 days postoperatively. Rihn et al. [14] observed 71% of patients suffered from dysphagia at follow-up 2 weeks. Most patients with dysphagia could resolve gradually within 3 months [1]. Therefore, local corticosteroid application may be found no significant effect on delayed dysphagia as compared with control group. The high incidence of dysphagia in early period is mainly attributed to PSTS which presents a tendency of spontaneous remission in postoperative course. Corticosteroid is an anti-inflammatory drug and can temper swelling resulting from cytotoxic or vasogenic pathology, likely including PSTS. In the studies evaluating the effect of local steroid on PSTS, Lee et al. [17] and Schroeder et al. [18] found local corticosteroid application significantly reduced PSTS. Edwards et al. [10] observed local corticosteroid application could significantly decrease dysphagia rates and magnitude following ACDF with BMP-2, a drug that is effective in promoting arthrodesis but also is a strong contributor to neck swelling and severe dysphagia [19, 20]. This result

Table 1 Summary of study characteristics

Authors and year	No. of Pts	Study design	Inclusion/exclusion criteria	Administration protocol of corticosteroid	Surgery	Instrument for assessment	Measurement of PSTS (yes/no)	Follow-up time points	Dysphagia (improve or not)
Edwards [10] (2016)	50	Prospect, RCT	Inclusion: Age18–70 1–3 levels ACDF Primary or revision surgery Exclusion: Non-degenerative pathology and OPLL	Steroid group: Collagen sponge saturated with corticosteroid Control group: No usage of corticosteroid	ACDF (BMP-2 was used intra-operatively)	Modified dysphagia scoring system	No	Postoperative days 1, 4, 7, 14, 28	Yes
Haws [11] (2018)	104	Prospect, RCT	Inclusion: Patients undergoing a primary 1- to 3-level ACDF due to myelopathy, radiculopathy, myeloradiculopathy, stenosis, herniated nucleus pulposus, degenerative disk disease, spondylosis, osteophytic complexes, and foraminal stenosis Exclusion: Allergies or other contraindications to medicines in the protocol including: existing history gastrointestinal bleeding, existing history of dysphagia, and current smokers Cervical spine trauma	Steroid group: Retropharyngeal corticosteroid plus systemic (IV) corticosteroid Control group: Systemic (IV) corticosteroid	ACDF	Quality of life in swallowing disorders (SWAL-QOL) questionnaire	Yes	6 weeks and 3 months postoperatively	No
Koreckij [12] (2016)	44	Retro, cohort	Inclusion: anterior cervical discectomy and fusion (ACDF) procedures for radiculopathy or myelopathy Exclusion: Single-level procedures, revision procedures, and procedures performed for trauma, infection, tumor, or autoimmune related diseases	Steroid group: Collagen sponge saturated with corticosteroid plus systemic corticosteroid Control group: Systemic corticosteroid	ACDF	Bazaz–Yoo dysphagia score and eat assessment tool (EAT-10)	Yes	6 weeks and 3 months postoperatively	Yes
Cancienne [13] (2016)	245754	Retro, cohort	Inclusion: Anterior cervical discectomy and fusion (ACDF) procedures for radiculopathy or myelopathy Exclusion: Single-level procedures, revision procedures, and procedures performed for trauma, infection, tumor, or autoimmune related diseases	Steroid group: local corticosteroid usage Control group: No usage of local corticosteroid	ACDF	NA	No	Within 90 days, Detailed intervals of follow-up evaluation were unclear	Yes
Jenkins [9] (2018)	50*	Prospect, RCT	Inclusion: Age ≥ 18 anterior cervical discectomy and fusion (ACDF) procedures for radiculopathy or myelopathy Exclusion: Procedures performed for trauma, infection, or tumor or revision procedures	Steroid group: Retropharyngeal corticosteroid Control group: No usage of corticosteroid	ACDF	Bazaz–Yoo dysphagia score and eat assessment tool (EAT-10)	No	1 day, 2 weeks, 6 weeks, 3 months, 6 months, and 1 year postoperatively	Yes

ACDF anterior cervical discectomy and fusion, *BMP-2* bone morphogenetic protein-2, *OPLL* ossification of posterior longitudinal ligament, *Prospect* prospective, *PSTS* prevertebral soft tissue swelling, *Pts* patients, *NA* not available, *RCT* randomized controlled trial, *Retro* retrospective

*Only data of local steroid group and control group were extracted

Table 2 Ranges and types of corticosteroid used

Studies	Corticosteroid group		Control group		Dysphagia (improve or not)
	Local usage Types and dosage	Systemic usage Types and dosage	Local usage Types and dosage	Systemic usage Types and dosage	
Edwards [10] (2016)	Depomedrol 40 mg	No	No	No	Yes
Haws [11] (2018)	Depomedrol 40 mg	Dexamethasone 10 mg	No	Dexamethasone 10 mg	No
Koreckij [12] (2016)	Methylprednisolone 80 mg	Decadron 10 mg	No	Decadron 10 mg	Yes
Cancienne [13] (2016)	Triamcinolone acetonide 1 mg or 10 mg Methylprednisolone acetate 20 mg, 40 mg, or 80 mg	No	No	No	Yes
Jenkins [9] (2018)	Triamcinolone 40 mg	No	No	No	Yes

may imply the strong efficacy of local corticosteroid on PSTS, even in the case of BMP-2 administration. Therefore, local corticosteroid application could effectively alleviate early dysphagia attributable to PSTS which mainly occurred in early postoperative period. As for lasting, steroid-unresponsive dysphagia, it may be ascribed to various causes other than PSTS, such as plate prominence [21, 22], scar formation [15], and laryngeal nerve injury [5]. Therefore, for patients with persistent postoperative dysphagia, especially who were given local corticosteroid intraoperatively, consideration of other causes of dysphagia, such as causes mentioned above other than PSTS, may be reasonable.

Complications associated with local corticosteroid application

Complications associated with local corticosteroid application include early complications, such wound infection, delayed wound healing, wound breakdown, and retropharyngeal abscess. This systematic review demonstrated that local

Table 3 Outcomes of postoperative dysphagia in detail

Authors and year	Instrument for assessment	Incidence and severity of dysphagia	Follow-up time points	Treatment group	Control
Edwards [10] (2016)	Modified dysphagia scoring system	Incidence	7 days	40.7%	78.3%
			14 days	33.3%	69.6%
		Severity	7 days	0.56 ± 0.751*	1.43 ± 1.04*
			14 days	0.52 ± 0.802*	1.39 ± 1.20*
Haws [11] (2018)	Quality of life in swallowing disorders (SWAL-QOL) questionnaire	Incidence	6 weeks	NA	NA
			3 months	NA	NA
		Severity	6 weeks	90.2 ± 12.1*	90.9 ± 11.5*
			3 months	90.6 ± 12.2*	93.8 ± 9.4*
Koreckij [12] (2016)	Bazaz–Yoo dysphagia score	Incidence	6 weeks	38.1%	77.3%
			3 months	23.8%	52.4%
		Severity	6 weeks	28.6%**	68.2%**
			3 months	9.5%**	22.8%**
Cancienne [13] (2016)	NA	Incidence	Within 90 days	16.5%	23.0%
		Severity	Within 90 days	NA	NA
Jenkins [9] (2018)	Bazaz–Yoo dysphagia score and eating assessment tool survey (EAT-10)	Incidence	2 weeks	14%	30%
			6 weeks	7%	29%
		Severity	2 weeks	0%**	15%**
			6 weeks	0%**	24%**

*Average score assessed by corresponding scale was reported to evaluated the severity of postoperative dysphagia

**The incidence of moderate or severe dysphagia was extracted to assess the effect of local steroid application on severity of dysphagia

administration of corticosteroid would not increase early corticosteroid-related complications, as was observed in 2325 patients who received local corticosteroid treatment without early complication occurring in the 5 studies. Similarly, Lee et al. [17] and Schroeder et al. [18] both did not find steroid-related complication in a total of 77 patients who were administered local corticosteroid intraoperatively following ACDF. Moreover, in contrast with systemic usage of corticosteroid, local corticosteroid application outperformed IV corticosteroid administration in terms of early severe dysphagia and has the advantage of low risk of systemic response and prevention of postoperative odynophagia [9, 18]. However, one concern over local corticosteroid application is the risk of long-term bone nonunion or pseudarthrosis. Although intravenous corticosteroid administration perioperatively showed to delay fusion, the study by Jeyamohan et al. [23] indicated there was no impact on final long-term fusion. In contrast, it is unclear whether local corticosteroid application decreases or delays the long-term fusion. To date, no large-sample study focused on the impact of local corticosteroid on long-term bone union after ACSS. A small-sample RCT study by Lee et al. [17] indicated that local steroid application did not cause bone nonunion in all 25 local steroid-treated patients during long-term follow-up time, while, on the contrary, 1 case in control group presented pseudarthrosis. Similarly, Schroeder et al. [18] also observed no cases of revision surgery for pseudarthrosis were identified in 52 patients received local depomedrol at follow-up 30 months. Of note, Lee et al. [24] reported that two cases developed esophageal perforation following anterior cervical fusion at 2 months and 11 months of follow-up, respectively, the cause of which the author thought was local corticosteroid application, but other factors may contribute esophageal perforation, such as surgical injury and plate migration. A systematic review performed by Halani et al. [25] showed the most common cause of esophageal perforation was "hardware failure," including plate migration, screw migration, and loosened plates and/or screws, which was responsible for 41% of perforations. The next common causes were chronic erosion by hardware and intraoperative injury. Therefore, the relationship between corticosteroid and esophageal perforation needs further analysis. Taken together, local corticosteroid application does not increase the risk of early potential complications, but it is necessary to evaluate the potential long-term complication associated with local corticosteroid application in future studies.

Limitation

The limitation of this systematic review lies in the large heterogeneity among the 5 studies in terms of administration protocol of steroid, instrument of dysphagia assessment, and follow-up time points. The difference regarding administration protocol of steroid among these studies mainly laid in the route and dosage of corticosteroid administration, which may result in different outcomes of postoperative dysphagia. As for the assessment tool of dysphagia, modified dysphagia scoring system, quality of life in swallowing disorders questionnaire (SWAL-QOL), Bazaz–Yoo dysphagia score or eat assessment tool (EAT-10) were used in the 5 studies, respectively. To date, there is no accepted instrument for assessing dysphagia after ACSS. Different assessment tool may contribute to the variation of dysphagia rates reported in these studies. Of these assessment tools, modified dysphagia scoring system and Bazaz–Yoo dysphagia score have yet to be validated and SWAL-QOL questionnaire and EAT-10 have ever validated in literatures, but SWAL-QOL questionnaire is cumbersome to complete, and therefore, it has not been widely used in clinical practice. In contrast, EAT-10 is more concise and has been developed into multiple languages version. Hence, EAT-10 may become a popular tool to assess dysphagia after ACSS in future. In addition, difference in follow-up time points among these studies is a large confounder resulting in different conclusions, because dysphasia mainly occurred in early period; studies that reported long-term results of corticosteroid may show no significant effect on dysphagia. Consequently, given the large heterogeneity among these studies, a planned comparison of these studies was not conducted. To improve comparability of incidence and severity of dysphagia between studies, it is important that future studies follow a standardized protocol of drug administration and assessment tool to evaluate dysphagia in early and long-term follow-up time. Finally, the variation of evidence level grade among these studies should remind us to take the final conclusion cautiously.

Conclusion

In conclusion, this review demonstrated local corticosteroid application can reduce the incidence and severity of dysphagia following ACSS without increasing early corticosteroid-related complications (recommendation: class IIb, level of evidence B). However, the surgeons should be cautious about potential delayed corticosteroid-related complications, such as pseudarthrosis and esophageal perforation, before further high-quality study is conducted to investigate whether these risks result from local corticosteroid application.

Compliance with ethical standards

Conflicts of interest The authors declare that they have no conflict of interest.

Ethical approval The study was approved by the institutional research ethics committee of Xuanwu Hospital.

Informed consent Not applicable.

Appendix

PubMed search (10-9-2018): (((((((deglutition disorders[MeSH Terms]) OR dysphagia[Title/Abstract]) OR soft tissue[Text Word]) OR edema[Text Word]) OR swelling[Text Word])) AND (((((((((steroid[MeSH Terms]) OR glucocorticoid[MeSH Terms]) OR corticosteroid[Text Word]) OR methylprednisolone[MeSH Terms]) OR methylprednisolone acetate[Text Word]) OR hydrocortisone[MeSH Terms]) OR cortisone[MeSH Terms]) OR hydroxycorticosteroid[MeSH Terms]) OR hexadecadrol[Text Word])) AND ((((((((((((((total disc replacement[MeSH Terms]) OR disc replacement, total[Title/Abstract]) OR replacement, total disc[Title/Abstract]) OR disk replacement[Title/Abstract]) OR artificial disk replacement[Title/Abstract]) OR disk replacement, artificial[Title/Abstract]) OR disc replacement[Title/Abstract]) OR artificial disc[Title/Abstract]) OR arthrodesis[MeSH Terms]) OR fusion [Title/Abstract]) OR diskectomy[MeSH Terms]) OR discectomy[Title/Abstract]) OR corpectomy[Title/Abstract]) OR decompression[Title/Abstract]) OR degenerat*[Text Word])

Embase search (10-9-2018): ('dysphagia'/exp OR 'deglutition disorder':ab,ti OR 'soft tissue':ab,ti OR 'edema':ab,ti OR 'swelling':ab,ti) AND ('steroid'/exp OR 'glucocorticoid'/exp OR 'corticosteroid'/exp OR 'methylprednisolone acetate'/exp OR 'hydrocortisone'/exp OR 'cortisone'/exp OR 'hydroxycorticosteroid'/exp OR 'hexadecadrol':ab,ti) AND ('total disc replacement'/exp OR 'disc replacement, total':ab,ti OR 'replacement, total disc':ab,ti OR 'disk replacement':ab,ti OR 'artificial disk replacement':ab,ti OR 'disk replacement, artificial':ab,ti OR 'disc replacement':ab,ti OR 'discectomy'/exp OR 'diskectomy':ab,ti OR 'corpectomy':ab,ti OR 'decompression':ab,ti OR 'degenerat*':ab,ti)

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