A SINGLE BLIND, PROSPECTIVE, RANDOMIZED CONTROLLED TRIAL ON THE EFFECT OF LOCAL STEROID APPLICATION VERSUS INTRAVENOUS STEROIDS ON DYSPHAGIA FOLLOWING ANTERIOR CERVICAL DISECTION AND FUSION

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Synopsis

Title	A single blind, prospective, randomized controlled trial on the effect of local steroid application versus intravenous steroids on dysphagia following anterior cervical discectomy and fusion (ACDF)
Short Title	Effect of local application vs. IV steroids on dysphagia after ACDF
Protocol Date	12/14/2015
Study Duration	2 years
Study Center(s)	Northwestern Memorial Faculty Foundation (NMFF), Northwestern University (NU), University of Wisconsin-Madison, OrthoCarolina Research Institute
Objectives	Local application of steroids in ACDF surgery will lead to decreased incidence of dysphagia compared to intravenous steroids or a control group
Number of Subjects	85 (randomized to group I (control group), group II (10 mg of intraoperative intravenous decadron), or group III (40mg of triamcinolone placed on cervical plate), i.e. 25 per group.
Diagnosis and Main Inclusion Criteria	Patients undergoing ACDF (single or multi-level) for the treatment of radiculopathy or myelopathy by Drs. Hsu, Patel, and Savage.

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1.0 INTRODUCTION - BACKGROUND AND RATIONALE

Dysphagia is a common complication after ACDF.[1] PSTS is also a natural sequela of ACDF and can lead to airway compromise among other complications.[2] Previous studies have demonstrated that administration of intravenous methylprednisolone (1mg/kg) after anterior cervical spine surgery reduced the incidence of pharyngolaryngeal lesions as identified by nasofibroscopic examination.[3] Lee et al. prospectively evaluated 50 patients and determined that local application of steroids in the retropharyngeal area following ACDF reduced PSTS and odynophagia as measured by the Visual Analogue Scale (VAS) and the Neck Disability Index (NDI) compared to a control group.[4] Furthermore, there were no adverse events/reactions from local application of steroid on a gel foam sponge in the setting of anterior spinal surgery. There are no studies in the current literature that investigate the incidence of dysphagia with application of local steroids after ACDF, nor are there any studies that stratify the efficacy of local steroids compared to intravenous steroids. There is also no current spine literature that directly compares the efficacy of intravenous steroids versus local steroids in the incidence of dysphagia or dysphonia. Our study will be the first in the literature to assess the efficacy of local steroids in reducing the incidence of dysphagia after anterior cervical spine surgery, and as a result, may improve patient outcomes after ACDF.

Dysphagia and dysphonia are common complications after anterior cervical spine surgery.[1] Despite their clinical importance, studies on the treatment and/or prevention of these complications are limited due to the lack of valid and reliable outcome measures. The majority of research is found in the otolaryngology literature and has focused on disease pathophysiology, diagnosis, and therapy.

The Bazaz score has been used in the spine literature to evaluate dysphagia after anterior cervical discectomy and fusion (ACDF).[5] This is a subjective questionnaire that has not been validated in the literature. Additionally, new patient-centered outcome measures, the Eating Assessment Tool (EAT-10) and Voice Handicap Index (VHI-10) have recently been developed, and in addition to the Bazaz score, have been shown to have excellent validity and reliability in the ENT patient population.[6] These instruments can be used to document the initial dysphagia or dysphonia severity and monitor the treatment response in people with a wide array of swallowing and voice disorders.

2.0 OBJECTIVES

- To determine if the use of steroids decreases the incidence of dysphasia after anterior cervical discectomy and fusion (ACDF).
- If steroids are useful, determine which method of steroid administration is most efficacious (IV versus local application).
- We hypothesize that local application of steroids in ACDF surgery will lead to a decreased incidence of dysphagia, in the postoperative period as compared to intravenous steroids or a control group.
- To evaluate the incidence of dysphonia, as measured by the Voice Handicap Index (VHI-10), as well as other validated outcome measures (NDI, VAS, EQ-5D).

3.0 SELECTION OF SUBJECTS

3.1 INCLUSION CRITERIA*:*

- All patients undergoing ACDF (single or multi-level) for the treatment of cervical radiculopathy or myelopathy with Drs. Hsu, Patel, and Savage.
- All subjects must have given signed, informed consent prior to registration on study.

3.2 EXCLUSION CRITERIA

- Patients undergoing revision surgery, any operations for trauma, infection, tumor
- Patients with general metabolic diseases such as rheumatoid arthritis, diabetes, chronic heart and renal diseases.

4.0 SUBJECT REGISTRATION

The subjects will be recruited by the PI, co-investigators, or authorized study staff at the orthopaedic surgery clinic or prior to their ACDF surgery in the pre-operative hold area in. The study will be reviewed with the subjects and they will be consented by the PI, co-investigator, or other authorized study staff.

Each collaborating site will be involved in subject recruitment, consent, and all data collection for any patients that are enrolled in the study at each respective site.

5.0 STUDY DESIGN & METHODS

We intend to prospectively evaluate 85 patients as part of a single blind, randomized controlled study. Subjects would be randomized to group I (control group, no steroid), group II (10 mg of intraoperative intravenous decadron with gel foam sponge placed on cervical plate), or group III (40mg of triamcinolone on gel foam sponge dabbed on the anterior cervical plate). Subjects will be blinded to the treatment arm. Randomization will take place on the day of surgery. 85 envelopes will be sealed, 25 of which will contain a document specifying “control”, “iv steroids”, or “steroid sponge”. The 75 envelopes will then be shuffled to create a random assortment. The circulating nurse in the OR will at random choose one envelop prior to the start of the operative procedure. This will in turn specify the treatment group for each patient.

There is no standard of care regarding the use of IV or local steroids in the setting of ACDF. Currently, the use of either IV or local steroids is at the discretion of the attending surgeon. To my knowledge, there are several spine surgeons at our institution that currently use no steroid, and others who use a combination of IV and/or local steroids.

The primary outcome measure is the incidence of dysphagia as measured by Eating Assessment Tool (EAT-10) and the Bazaz score. The patients will prospectively fill out these surveys preoperatively, post-operative day 1, week 2, week 6, month 3, month 6, and 1 year as a measure of dysphagia. The standard of care is to see patients in the office at 2 weeks, 6 weeks, 3 months, 6 months, and 1 year after surgery, and therefore, no extra visits will be necessary for this study. X-rays will be taken at 6 weeks, 3

months, and 12 months post-op, which is the current standard of care. No additional x-rays will be obtained.

A secondary outcome measure will be the incidence of dysphonia, as measured by the Voice Handicap Index (VHI-10), as well as other validated outcome measures (NDI, VAS, EQ-5D). The questionnaires will take approximately 20 minutes to complete and will be administered in the hospital, during the post-operative clinic visits with the surgeon, or over the phone. The surgeons will also listen to the patient's voice at these different time points and comment on dysphonia as being absent, mild, moderate, or severe.

Additionally, a chart review will be performed from11/01/2013 to 12/30/2016 from NMH Medical records (PRIMES, Cerner PowerChart) and NMFF Medical Records (EpicCare, IDX/GE Centricity) to obtain the following data: Complications such as infection, post-operative hematoma, airway compromise, and recurrent laryngeal nerve palsy. All data collected from chart review will be de-identified and noted on the Data Collection Form. Each subject will be assigned a study number and all data will be linked to that number using the Coded Identifier List. The PI will identify which charts will be reviewed. The chart review will be performed by the PI, co-investigators, or authorized study coordinator.

There are potential physical risks from being in this study. The use of steroids may have an adverse effect on wound healing and/or transiently elevate blood sugar. There have been no documented wound complications from using either IV or local steroids in the setting of ACDF. Furthermore, we purposely excluded patients with a history of diabetes or other endocrine disorder in an attempt to minimize this potential side-effect or complication. Another possible risk related with participation in this study is the loss of privacy. To reduce these risks, all of the information collected will be de-identified and stored in a password protected file on a password protected computer. Additionally, some of the questions asked in the surveys may be upsetting, or the subject may feel uncomfortable answering them. If the subject does not wish to answer a question, they may skip it and go to the next question.

6.0 STATISTICAL PLAN

We will use T score or ANOVA to compare EAT-10 scores, VHI scores, andEQ-5D, and Chi square for subjective findings. The P value will be set at 0.05.

A power analysis was performed to determine the sample size needed. Based on previous studies evaluating the EAT-10 in normal patients and those with dysphasia the analysis concluded: with total sample size 85 (Group I: 25, Group II: 25, Group III: 25) and estimated standard deviation of EAT-10 as 12.7, **power = 0.92**

Drs. Savage, Patel, and Hsu, perform approximately 6 ACDFs a month. This would allow us to collect our proposed sample size in approximately 12-14 months.

7.0 DATA COLLECTION & RECORD KEEPING

All information regarding the nature of the proposed investigation provided to the investigator (with the exception of information required by law or regulations to be disclosed to the IRB, the subject, or the appropriate regulatory authority) will be kept in confidence by the investigator. All personal information will be treated as strictly confidential and not made publicly available. All records and appendices are stored in separate locked filling cabinets as well as a password protected computers which are accessed only by the Principal Investigator, co-investigator, and authorized study staff. All identifiable data will be destroyed a year after the study is complete.

9.0 REFERENCES

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APPENDICES

CODED IDENTIFIER FORM

Unique subject identifier	Last Name	First Name	MRN
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DATA COLLECTION FORM

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