

Intranasal Medication Delivery Utilizing EDS After Limited ESS in Cadavers



Abstract

Introduction: One goal of endoscopic sinus surgery (ESS) is to facilitate medication delivery to the sinuses, optimizing chronic rhinosinusitis (CRS) management. Limited ESS may achieve this without the need for more comprehensive surgical approaches. Exhalation delivery systems (EDS) have shown safety and efficacy for topical steroid delivery in CRS patients. This study seeks to evaluate sinonasal topical penetration by EDS compared to conventional nasal sprays (NS) after limited ESS in cadavers.

Methods: Eight cadavers underwent limited ESS, including uncinectomy, maxillary antrostomy, and anterior ethmoidectomy. Fluorescein dye was delivered via EDS and NS. Images of middle turbinate (MT), maxillary sinus (MS), and anterior ethmoid (AE) subsites were captured endoscopically and rated from 0 (no staining) to 3 (heavy staining) by 7 rhinologists. Ratings were averaged for each subsite. Differences in staining between EDS and NS were assessed using Wilcoxon signed-rank tests.

Results: Average AE staining was greater in EDS specimens compared to NS (1.438±0.785 vs. 0.911±0.843, p=0.012). In a summed composite measure of post-ESS staining in MT, MS, and AE subsites, staining score was greater in EDS specimens compared to NS (3.589±1.560 vs. 2.813±1.680, p=0.044). Inter-rater reliability was excellent with an ICC of 0.956 (95% CI: 0.931, 0.972).

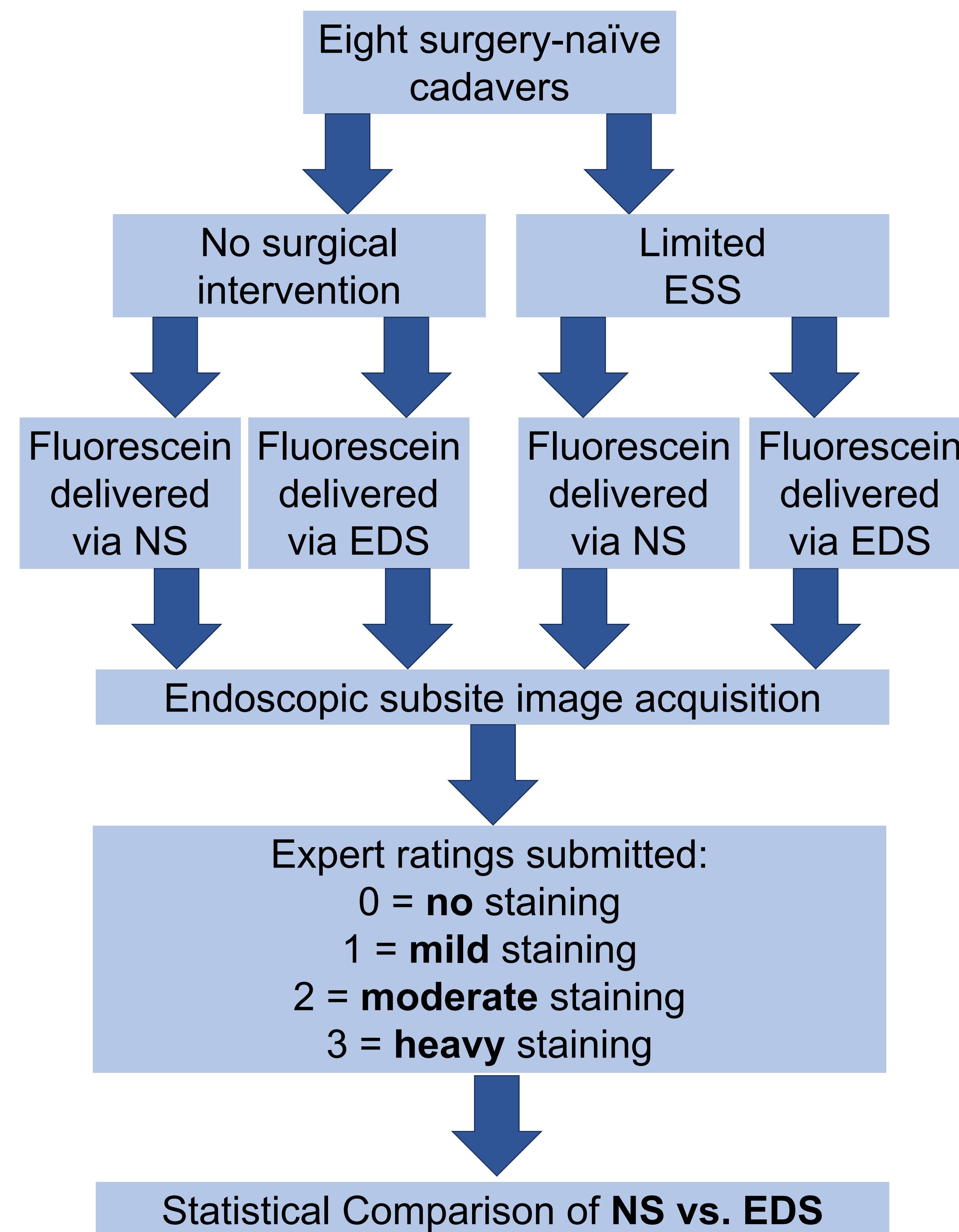
Conclusions: These findings demonstrate a significant increase in EDS medication delivery to anatomic subsites following limited ESS. This increase is reflected in the composite score, with the main contribution from staining in the AE region. Patients who undergo limited ESS for CRS treatment may benefit clinically more from EDS than NS medication delivery, where additional research would provide requisite insight into true clinical implications in this population.

Introduction

Traditionally, INCS have been administered via a conventional nasal spray (NS) to address CRS disease. However, NS frequently does not pass through the nasal valve, with scintigraphic scanning showing that up to 80% of spray may not reach the ciliated nasal cavity.¹ Nasal drops as an administration method showed improved drug delivery beyond the nasal valve¹; however, this method is cumbersome for the patient and could result in systemic absorption of corticosteroids thus posing increased risk for side effects. One of the first aerosolizing devices focused on improving drug delivery through the use of an exhalational delivery system (EDS) – otherwise known as bidirectional delivery.²⁻³ The EDS mechanism functions by: 1) exhaling into a mouthpiece to create an airtight seal of the soft palate (concentrating medication in the nasal cavity and preventing transfer to the lungs), 2) increase intranasal pressures to expand inflamed passages, and 3) “floating” medication throughout the entire nasal cavity with air exiting through the contralateral nostril.²⁻⁴

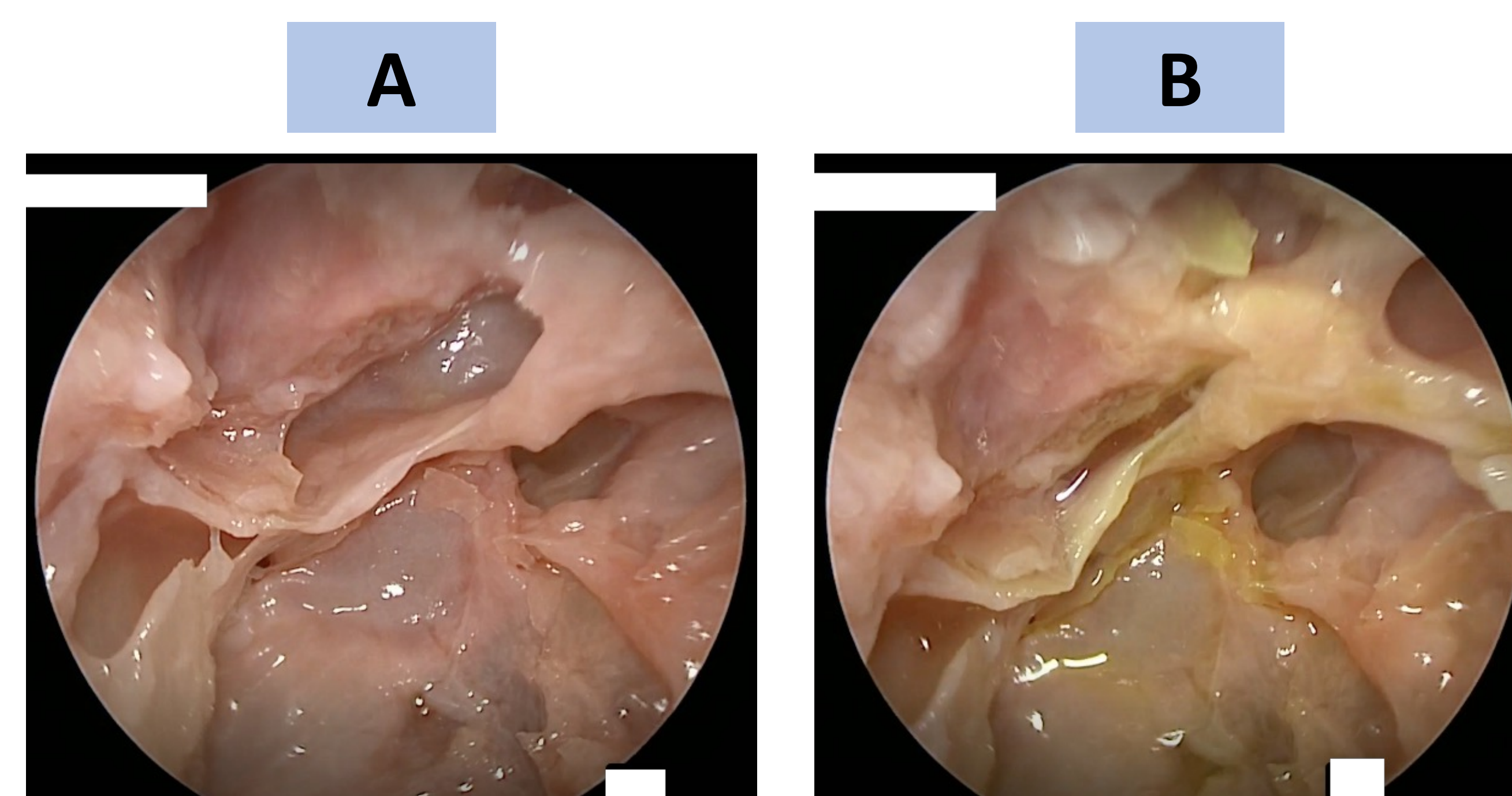
There have been several recent studies examining the efficacy of fluticasone EDS (EDS-FLU) in patients with CRSwNP.⁴⁻⁷ Those studies that examined outcomes of EDS-FLU versus EDS-placebo concluded that EDS-FLU treated patients had improved quality of life and endoscopic nasal polyp scores in addition to improvement in self-reported olfaction.⁸

Methods



Results

Figure 1. A: Anterior ethmoid sinuses after limited ESS sprayed with NS; B: Anterior ethmoid sinuses after limited ESS sprayed with NS



Results Cont.

Table 1. Mean fluorescein dye staining by anatomic site

Surgical Group	Delivery Method	Middle turbinate	Maxillary Sinus	Anterior Ethmoid	Composite Sum
No Surgery	NS	1.305±1.061	-	-	-
	EDS	1.321±0.742	-	-	-
Limited ESS	NS	1.518±0.758	0.384±0.518	0.911±0.843	2.813
	EDS	1.670±0.688	0.482±0.549	1.438±0.785	3.589

Discussion

There are several delivery methods beyond conventional NS used for topical INCS administration in CRS. High volume irrigation devices have superior penetration of the nasal valve when compared to NS.⁹ However, several cadaveric studies show that head positioning is paramount for ideal drug distribution, and improper positioning may lead to inferior deposition throughout the sinonasal cavity but especially to the frontal sinus.¹⁰⁻¹¹ Importantly, Djupesland et al.¹² conducted a study using silicone casts of the sinonasal cavities from a patient after Draf II and Draf III procedures in which they assessed the degree of liquid deposition after NS, EDS, and high-volume, low-flow (HVLF) delivery with the head tilted to either 45° or 90°. They found that EDS deposited throughout the entire sinonasal cavity after Draf III whereas conventional NS deposited only in the anterior nasal segments and HVLF did not reach the roof and posterior wall of the ethmoid region even with the head tilted to 90°. ¹² This study provides further evidence that EDS deposits substrate into anatomically isolated regions like the ethmoid, emphasizing the improved distribution with EDS when compared to other effective delivery methods like HVLF or NS. Superior distribution without the need for precise head positioning offers an increase in efficacy and convenience for patients with CRS.

This study is not without limitations. Cadaveric models do not recapitulate variation in head positioning, administration method, or individual turbinate vasodilation as would be expected in a real clinical environment. Additionally, we are unable to assess the dynamics of these distribution methods and how they are affected by breathing, mucociliary clearance, and varying degrees of inflammation.

Conclusions

In the present study, EDS shows an overall superior sinonasal penetration into MT, MS, and AE subsites when compared to NS. The AE subsite showed particularly greater deposition for EDS administered dye. These findings provide structural evidence for improved sinonasal deposition via the EDS dispersion method when compared to conventional NS.

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