Radiofrequency Volumetric Tissue Reduction of the Inferior Turbinate in a Sheep Model

Kiran Kakarala, MD; William C. Faquin, MD, PhD; Michael J. Cunningham, MD

Objectives/Hypothesis: To validate the sheep model for endoscopic nasal surgery, and to utilize this model to compare the immediate and early postoperative histopathologic effects of four electrosurgical turbinate reduction techniques.

Study Design: Pilot comparative study of electrosurgical devices for inferior turbinate reduction using a sheep model.

Methods: Three radiofrequency devices (one monopolar and two bipolar) were compared to monopolar electrosurgery in a sheep model of inferior turbinate reduction. Procedures were performed according to device manufacturer guidelines using standard endoscopic instruments. Normative acoustic rhinometry data were obtained for the sheep model. Histopathologic analysis of turbinate specimens was performed at postoperative day 0 and 21.

Results: Turbinate reduction was performed on seven sheep, one procedure on each side, yielding 14 turbinate specimens. Acoustic rhinometry was validated in the sheep model and demonstrated increased nasal volumes following decongestion and turbinate reduction. Submucosal destruction of glands and venous sinusoids and replacement with fibrosis were demonstrated as a common mechanism of action for all four electrosurgical devices. Epithelial disruption was seen with all devices on postoperative day 0. Squamous metaplasia and normal respiratory epithelial regeneration were documented variably between devices at postoperative day 21.

Conclusions: The sheep model is useful for study of both the anatomic and histopathologic effects of endonasal procedures. Standard endoscopic instruments and acoustic rhinometry can be used in this model with reproducible results. In this pilot animal study, radiofrequency devices for inferior turbinate reduction demonstrated greater preservation of normal nasal mucosal respiratory epithelium when compared to monopolar electrocautery.

Key Words: Sinonasal, general otolaryngology, allergy.

Level of Evidence: 2c

INTRODUCTION

Perhaps no surgical procedure in otolaryngology better demonstrates the proliferation of varied technologies to achieve a common goal than the reduction of the inferior turbinate. The use of electrosurgery, radiofrequency volumetric tissue reduction (RFVTR), laser, ultrasound, and microdebrider have all been reported.1–6 Within the category of RFVTR alone, three instruments are currently available for use in clinical practice.7–10 There are several clinical studies and review articles assessing the safety and clinical effectiveness of these various devices.6–12 There is, however, a paucity of information available on the mechanism of action and histopathologic effects of these procedures on the turbinate tissue. Such data are prerequisite to understanding the clinical application of these techniques and comparing the outcomes achieved by them. For example, a possible advantage of radiofrequency devices over monopolar electrocautery is the preservation of normal nasal mucosa structure and function. Although there are some functional data from clinical trials to support this claim, the histopathologic evidence is limited.6

The relative scarcity of histopathologic data reflects the practical and ethical concerns of obtaining turbinate tissue from patients following a minimally invasive endonasal turbinate reduction procedure. The sheep model has been investigated for the study of endonasal procedures and is particularly useful for assessing histopathology and wound healing of the sinonasal mucosa.13–16 This model accommodates the use of standard endoscopic sinus surgery equipment, allowing for accurate simulation of clinical procedures.

The goals of this study were to validate a turbinate reduction model in sheep and to study the mechanism of action and histopathologic effects of RFVTR devices in comparison to monopolar electrocautery. We report our findings regarding normative acoustic rhinometry (AR) data for this sheep model, as well as the immediate and early postoperative histopathologic changes of turbinate...
tissue following reduction with monopolar electrosurgery or RFVTR.

MATERIALS AND METHODS
This study was approved by the Institutional Animal Care and Use Committee of the Massachusetts Eye and Ear Infirmary. Procedures followed United States federal guidelines for the care and treatment of experimental animals.

Animals/Anesthesia
Seven 1-year-old female sheep weighing between 35 and 45 kg formed the study population. Animals were fasted for 24 hours prior to procedures. Anesthesia was induced with thiotetinal sodium 7.5 mg/kg intravenously, and maintained with 1% to 3% inhalational isoflurane via oral endotracheal tube intubation.

Surgical Devices
The radiofrequency devices used in this study included two bipolar and one monopolar device. The bipolar radiofrequency devices were the Coblator II with ReFlex Ultra 45 handpiece (ArthroCare ENT, Austin, TX) and the CelonLab ENT (Celon AG, Teltow, Germany). The monopolar radiofrequency device was the Somnoplasty G3 Workstation with turbinate handpiece (Gyrus ACMI, Bartlett, TN). The monopolar electrosurgical device used was the Force FX with handswitching pencil (E2515) and needle electrode (E1552; Valleylab, Boulder, CO).

Protocol/Surgical Procedures
Each animal underwent one procedure on each side of the nose, yielding a total of 14 turbinate specimens. A pilot study with three animals was initially performed in which the four turbinate reduction devices were tested and calibrated for the sheep model. The remaining four animals were then used to further study the immediate and early (21 day) postoperative effects of the devices. Turbinates from two animals were harvested immediately following the turbinate reduction procedures, and turbinates from two animals were harvested at 21 days postoperatively.

AR measurements were obtained using the EccoVision Acoustic Rhinometer (Sleep Group Solutions, North Miami Beach, FL). Baseline measurements of nasal volume and cross-sectional area were obtained for four animals. Four sets of measurements were then obtained for two animals: baseline preprocedure, postdecongestion with oxymetazoline nasal spray, 21 days post-turbinate reduction procedure, and post-turbinate specimen harvest (turbinectomy). Additionally, a 0° rigid nasal endoscope was used to obtain intranasal turbinate photographs preprocedure, immediately postprocedure, and at 21 days postprocedure in two animals.

The surgical procedures were conducted as follows. For Coblation bipolar radiofrequency reduction, the ablation setting was set at a power level of 5. Using endoscopic visualization, the needle tip of the probe was inserted into the turbinate submucosally parallel to the bone, and the device was activated for 10 seconds. For Celon bipolar radiofrequency reduction, the ablation setting was set at 15 W, and the needle tip of the probe was inserted into the turbinate as described above. The device was activated until the auto-stop power control feature engaged (turning off the device automatically when appropriate tissue impedance was reached). For Somnoplasty monopolar radiofrequency ablation, a grounding pad was applied to the sheep on a shaved area of skin. The device was set to deliver 500 J total energy. The needle tip of the probe was inserted into the turbinate as described above, and then the device was activated until energy delivery was complete. For monopolar electrosurgery (electrocautery), the device was set to 20 W on the coagulation setting. The needle tip was inserted into the turbinate as described above, and the device was activated for 10 seconds. For all four devices, the procedure was performed a total of three times to treat the anterior, middle, and posterior portions of the turbinate.

Histopathologic Comparison
Specimens were fixed in formalin and embedded in paraffin. The paraffin blocks were serially sectioned perpendicular to the long axis of the turbinate. Slides were stained with hematoxylin and eosin, and reviewed by a pathologist (W.C.F.) blinded to the surgical procedure. A qualitative, descriptive histopathologic assessment with respect to immediate (postoperative day 0) and early (postoperative day 21) submucosal and mucosal tissue effects was performed.

RESULTS
Nasal Endoscopy Photographs
Representative nasal endoscopy photographs are shown in Figures 1 and 2. Figure 1A is an untreated left nasal cavity demonstrating prominent mucosal edema of

![Fig. 1. (A) Normal sheep left nasal cavity with turbinate demonstrating prominent mucosal edema (arrow). (B) Left nasal cavity following partial turbinectomy demonstrating concha bullosa (arrow) as normal anatomy of the sheep turbinate.](image-url)
the turbinate, which was seen in all sheep prior to treatment. Figure 1B shows a left nasal cavity following partial turbinectomy to harvest the turbinate specimen; it demonstrates concha bullosa of the turbinate, which is also a normal feature of the sheep nasal anatomy. Figure 2A shows a right nasal cavity 21 days following turbinectomy via monopolar electrosurgery demonstrating prominent nasal crusting and partial turbinate necrosis. Figure 2B shows a right nasal cavity 21 days following turbinectomy reduction via RFVTR device (Celon), demonstrating mild coagulum and turbinate reduction with grossly intact mucosa.

AR

AR data are shown in Tables I and II. Baseline nasal volume and cross-sectional area measurements were obtained in four sheep (Table I), demonstrating consistency of measurements across subject animals. Table II demonstrates increases in both nasal cross-sectional area and nasal volume status after medical decongestion, status after turbinectomy reduction at 21 days postprocedure, and status after turbinectomy harvest. These findings were found to be consistent and proportional with anatomic findings on nasal endoscopy. For example, decongestion and turbinectomy reduction yielded modest increases in nasal volume, whereas turbinate removal more than doubled the measured nasal volumes and cross-sectional areas.

Histopathology

Control specimen. Consistent with endoscopic findings, the sheep turbinite was histopathologically found to uniformly contain a concha bullosa (Fig. 3A). Sheep nasal mucosa was identical to human nasal mucosa, consisting of pseudostratified ciliated columnar epithelium (Fig. 3B). Submucosal tissue contained primarily venous sinuses and seromucinous glands with a loose connective tissue stroma (Fig. 3). Larger venous sinuses extended more deeply toward the turbinite bone, whereas smaller, thin-walled blood vessels extended toward the mucosa.

Postoperative day 0. All devices demonstrated coagulative destruction of venous sinuses and seromucinous glands as a common mechanism of action for turbinectomy reduction (Fig. 4). All devices caused some degree of mucosal disruption. However, the qualitative degree of mucosal disruption was greatest with monopolar electrosurgery, which demonstrated large areas of complete mucosal shedding (Fig. 4A). The RFVTR devices achieved submucosal coagulation with more focal disruption of overlying mucosa and overall greater preservation of normal pseudostratified ciliated columnar mucosa (Fig. 4B).

Postoperative day 21. Replacement of submucosal venous sinuses, seromucinous glands, and loose connective tissue with fibrosis was seen as a common mechanism of action in both monopolar electrosurgery and RFVTR (Fig. 5). Monopolar electrosurgery additionally caused marked metaplasia of mucosa characterized by replacement of respiratory epithelium with robust squamous mucosa. There were also sizeable areas of complete mucosal loss. All three RFVTR devices also demonstrated focal areas of squamous metaplasia (Fig. 5); however, qualitatively greater preservation of normal nasal mucosa was noted in comparison to monopolar electrosurgery.

DISCUSSION

This study provides further validation of the utility of the sheep model in studying endonasal surgical procedures. Previous studies performed outside of the United States have demonstrated that sheep nasal anatomy is favorable for the use of standard endoscopic sinus
surgery instrumentation. Coronal computed tomography imaging of sheep sinonasal anatomy has demonstrated features similar to humans, especially with regard to the turbinates.13 Additionally, sheep nasal mucosa and sinonasal physiology have been shown to be analogous to humans.14,15 Due to the limitations of obtaining tissue from humans, the sheep model thus provides a viable option for the study of the histopathologic effects of endonasal procedures. This study expands the utility of the sheep model by demonstrating the ability to obtain endoscopic photo documentation of procedures and by providing normative AR data.

Using acoustic reflections, AR provides data on nasal volume and cross-sectional area in a rapid and noninvasive manner.17 Normative data have been described for humans, and AR measurements are often included in clinical trials of endonasal surgical procedures.17,18 Koss et al. demonstrated the utility of this technique in the study of nasal congestion in a dog model.19 Our study demonstrates that AR yields reliable measurements of nasal cross-sectional area and volume in sheep. The standard acoustic rhinometer did not require modification for use with this sheep model. Expected increases in nasal volume and cross-sectional area were seen following decongestion, turbinate reduction, and turbinate harvest, and the magnitude of enlargement was consistent with endoscopic findings. Future studies could make use of AR data to provide quantitative measurements of the changes in nasal anatomy that occur following endonasal procedures such as turbinate reduction.

With respect to histopathologic changes observed in turbinate tissue following the turbinate reduction, this study demonstrated three main findings. First, electro-surgical devices effect turbinate reduction via a common mechanism involving coagulation of venous sinusoids and seromucinous glands and the induction of submucosal fibrosis. Replacement of venous sinusoids and loose connective tissue with fibrosis prevents the engorgement of turbinate tissue, which causes nasal obstruction. This finding confirms the limited data available in the literature from sheep and human studies of turbinate reduction histopathology.4,16,20,21

Second, although all devices cause immediate mucosal disruption, the radiofrequency devices demonstrated qualitatively greater preservation of normal sinonasal mucosa. The pathogenesis of this finding can perhaps be understood by analyzing the differences between devices with respect to energy delivery. All of the devices tested in this study use heat energy to cause coagulative necrosis; however, they differ in the delivery mechanism. Whereas monopolar electrocautery devices can reach temperatures of up to 800°C, radiofrequency devices operate at temperatures regulated between 60 and 90°C.9,22 Collateral damage to surrounding tissues, such as mucosa, might be limited by lower operating temperatures, achieved by precisely regulating energy delivery by the device. It should be noted that the amount of energy delivered by the four devices in this study was not identical. We employed power settings that have been recommended in the literature for turbinate reduction procedures using these devices. Different power settings and surgical techniques such as number of passes and total time of application will influence the total energy delivered by the device and thus the effects on the target tissue. For example, the Somnoplasty

<table>
<thead>
<tr>
<th>Time</th>
<th>Volume, cc</th>
<th>CSA1, cm²</th>
<th>CSA2, cm²</th>
<th>CSA3, cm²</th>
</tr>
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<tbody>
<tr>
<td>Pre-operative</td>
<td>2.71 (± .43)</td>
<td>0.28 (± .05)</td>
<td>0.51 (± 0.11)</td>
<td>0.91 (± 0.17)</td>
</tr>
<tr>
<td>Post-decongestant</td>
<td>3.42 (± 1.07)</td>
<td>0.034 (± 0.07)</td>
<td>0.75 (± 0.33)</td>
<td>1.05 (± 0.27)</td>
</tr>
<tr>
<td>Post-turbinate reduction, 21 days</td>
<td>4.29 (± 2.05)</td>
<td>0.42 (± 0.11)</td>
<td>0.76 (± 0.25)</td>
<td>1.75 (± 1.25)</td>
</tr>
<tr>
<td>Post-turbinate harvest</td>
<td>8.70 (± 2.27)</td>
<td>0.80 (± 0.23)</td>
<td>1.96 (± 0.58)</td>
<td>2.92 (± 0.63)</td>
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CSA = cross-sectional area.

Fig. 3. (A) Concha bullosa (star), extensive submucosal venous sinusoids, and seromucinous glands (hematoxylin and eosin [H&E]; original magnification, ×100). (B) Pseudostratified columnar epithelium identical to human (arrowhead), with seromucinous gland (arrow), and venous sinusoid (star; H&E; original magnification, ×400).
device was set to deliver 500 J of energy, whereas the electrocautery device was used at a setting of 20 W for 3 passes of 10 seconds each, yielding a total energy of 600 J delivered to the turbinate. Such differences between devices in this pilot study need to be taken into consideration when judging experimental results.

Third, all devices caused some degree of squamous metaplasia of the nasal mucosa, as demonstrated in turbinate specimens obtained 21 days postprocedure. Again, this finding was most pronounced with monopolar electrosurgery, but was also seen with the three radiofrequency devices. Gindros et al. observed similar squamous metaplasia in human nasal mucosa following monopolar electrocautery, Coblation bipolar radiofrequency, and ultrasound turbinate reduction.4 There was no comment on the comparative amounts of metaplasia seen between devices, perhaps due to the limited nature of the biopsy specimens obtained from human subjects. Coste et al. obtained brush biopsies from turbinates treated with monopolar radiofrequency and showed that although ciliated mucosal cells predominated, moderate amounts of squamous cells were also seen at 7 and 60 days postprocedure.6 The pathogenesis of this squamous metaplasia might be understood by analyzing the normal makeup of the inferior turbinate mucosa. Berger et al. demonstrated that the anterior portion of the normal inferior turbinate is covered with squamous epithelium, and that transitional epithelium is found in islands scattered throughout the turbinate.23 It is possible that this squamous epithelium develops as a protective response to trauma. Thus, all energy-based devices may induce this squamous metaplasia from both direct physical trauma to the turbinate mucosa and heat-based trauma from the submucosal delivery of energy. The zone of injury induced by monopolar electrocautery may include more of the mucosal surface in comparison to that induced by radiofrequency devices.

In summary, all devices coagulated submucosal blood vessels, seromucinous glands, and connective tissue, and induced a fibrotic response as a common mechanism of action for turbinate reduction. Radiofrequency devices demonstrated greater preservation of normal nasal respiratory mucosa compared to monopolar electrosurgery. Squamous metaplasia was demonstrated at 21 days postprocedure for all devices tested in this study. These histopathologic findings should be correlated with clinical experience to understand differences between devices with respect to clinical effectiveness and complications. Such findings may also guide the development of future turbinate reduction devices.

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Fig. 4. (A) Monopolar electrocautery postoperative day (POD) 0 (hematoxylin and eosin [H&E]; original magnification, ×100): all devices cause coagulation of venous sinusoids and seromucinous glands (arrow), with some disruption of overlying mucosa (star). (B) Radiofrequency volumetric tissue reduction (Coblation) POD 0 (H&E; original magnification, ×100): submucosal coagulation of venous sinusoids and seromucinous glands with relative preservation of overlying respiratory mucosa (arrow).

Fig. 5. (A) Radiofrequency volumetric tissue reduction (RFVTR; Coblation) postoperative day (POD) 21 (hematoxylin and eosin [H&E]; original magnification, ×100): squamous metaplasia of mucosa (arrow) was seen most markedly with monopolar electrocautery, but was seen with all devices to varying degrees at POD 21. (B) RFVTR (Somnoplasty) POD 21 (H&E; original magnification, ×400): squamous metaplasia (arrow) with underlying fibrosis (star).
CONCLUSION

The sheep provides a useful model for study of both the airway enhancement and histopathologic effects of endonasal procedures. Standard endoscopic instruments and AR can be used in this model with reproducible results. In this pilot animal study, radiofrequency devices for inferior turbinate reduction demonstrated greater preservation of normal nasal mucosal respiratory epithelium when compared to monopolar electrosurgery.

BIBLIOGRAPHY


