Microscopic endonasal access in pituitary surgery for tumour removal: eight-year review of nasal complications

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Abstract

Introduction
Trans-sphenoidal pituitary resection is possible via the traditional microscopic trans-septal approach or newer endoscopic transnasal approach. There is little in the literature to describe the nasal complications of the endonasal microscopic resection of pituitary lesions. We describe our experience of a single surgeon series and specifically the nasal complications from this method.

Method
We preformed an 8-year retrospective case notes review of transnasal endoscopic resections of 70 pituitary tumours. The data were collected on a proforma developed after consultation with a multidisciplinary team and validated independently by random interval analysis.

Results
Gross tumour removal rate was achieved in 77.1% (n = 54/70) cases by 24 months follow-up. One patient experienced a purulent nasal discharge, which required antibiotic intervention, whilst another had persistent maxillary nerve damage with paraesthesia. No patient experienced persistent epistaxis, septal perforation, anosmia, cerebrospinal fluid leaks or meningitis. Unfortunately, one patient succumbed from the consequences of internal carotid artery damage.

Conclusion
Nasal complication rates from this method were low. A microscope can be successfully used in an endonasal approach to the sella on its own. It can also be a useful adjunct to the endoscope and this skill should not be forgotten by ear, nose and throat surgeons and neurosurgeons. It appears that the method of approaching the sella (transnasal vs trans-septal) rather than the instrument used helps to determine the rate of nasal complications.

Introduction
There have been many advances in approaches to the pituitary gland over the past century. Having been first performed transcranially4, whenever the anatomical configuration of the condition allows, the preferred approach for lesions of the sella is trans-sphenoidal (Figure 1). Access to the sphenoid sinus has generally been performed using a midline submucosal resection. This trans-septal route uses either a sublabial approach to the septum or an incision in the mucosa commencing within the anterior nares; both techniques usually involve resection of at least part of the nasal septum. Furthermore, even in experienced hands, the incidence of nasal septum perforation is reported to be 3.3%. A direct transnasal approach to the sphenoid sinus avoids potential complications of submucosal resection and, in case of a translabial approach, removal of the maxillary spine. To assess the benefits of the direct transnasal approach, a retrospective study of complications associated with this procedure was undertaken.

Access to the pituitary gland had been microscopic and via the trans-septal route following the work of Hardy in the 1960s and 1970s5,6. In recent years, however, the endoscope has started to establish itself as the option of choice because of improved visualisation offered to the operating surgeon and excellent short-term results. However, long-term resection results of this technique are still awaited. Nevertheless, it carries a

Footnotes
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clear advantage in the published data thus far over the microscopic transseptal technique, with equivalent or better results and fewer complications. However, majority of the comparative studies have not compared endoscopic transnasal technique with microscopic transnasal technique, as the endoscopic technique has its own disadvantages.

Both techniques usually involve resection of at least part of the nasal septum. Trauma to the nose and subsequent complications can form a significant basis of morbidity for patients undergoing pituitary surgery. They may not be perceived as being as important as other life-threatening complications of sellar and parasellar regions, but they can leave the patients with symptoms that often will require ear, nose and throat (ENT) input. Even in experienced hands, the incidence of nasal septum perforation is reported to be 3.3%. We present our retrospective series of the complications experienced by the direct transnasal microscopic approach with no endoscopic assistance. This is the largest case series of its kind in Europe and the fifth largest overall.

Methods and materials
All patients presenting with pituitary tumours (Figure 2) were managed in a multidisciplinary environment with teams including neuroendocrinology specialists with a neurosurgeon and two endocrinologists, supported by Departments of Neuropathology, Neuroradiology and Ophthalmology. The records of 70 consecutive patients undergoing pituitary surgery via the transnasal route by a single surgeon during the preceding 8 years were obtained. There were 42 males and 28 females. The mean age was 56 years (range, 19–85 years). There were 66 pituitary adenomas, 3 craniopharyngiomas and 1 meningioma.

Pre-operative imaging included coronal magnetic resonance imaging (MRI) in all cases (Figures 3 and 4). In many cases, computed tomography (CT) imaging was also available. In addition to providing confirmation that a trans-sphenoidal approach was appropriate, the coronal images (MRI or CT) were used to define the position and characteristics of the sphenoid septum, an essential landmark in establishing the position of the midline pre-operatively. Cefuroxime (1.5 g) was intravenously administered routinely with induction, together with hydrocortisone (100 mg).

Once positioned on the operating table, the anterior nasal mucosa of both nostrils was liberally coated with benzoylmethylecgonine paste. The face was prepared using aqueous betadine solution and the right thigh was prepared, in expectation should a fascia lata graft be required. Surgery was undertaken via the right anterior nares in all cases using the operating microscope and with lateral screening using an image intensifier (Figures 5–7). The sphenoid sinus was approached via a direct transnasal approach. Any nasal polyps encountered were reduced using bipolar coagulation or microdebrider. After coagulating the nasal mucosa overlying the right side of the vomer, a posterior right septotomy ± posterior septectomy was performed.
Muco-periosteal flaps were raised on both sides through the right sided posterior incision to expose both sides of the vomer. Whenever accessible, further access to the sphenoid sinus would be obtained via the aditus located high up to the right of the midline. Exposure would then be facilitated using pituitary rongeurs or, particularly in acromegalics when the bone may be hyperostotic, a small hammer and chisel. Use of a high-speed hand drill for this stage of the procedure has been advocated but was not used in this series. After gaining access to the sphenoid sinus, its mucosa would be stripped and the sella floor opened. The procedure was undertaken under X-ray control.

At the conclusion of the procedure, a Valsalva manoeuvre was performed in all cases. If cerebrospinal fluid (CSF) leakage was evident, then a fascia lata graft was used to seal the sella floor supplemented with tissue glue. In such cases, adjunctive spinal drainage would be used for 3 days post-operatively. Prior to closure (and, where used, insertion of the myofascial graft), meticulous haemostasis would be established within the pituitary fossa, often by packing and gentle irrigation with saline and/or hydrogen peroxide, and always by patient observation. After removing the retractor from the right anterior nares, a Killian’s retractor would be passed into the left side to reposition the septum. In three cases, a small releasing incision was required in the right anterior nares to pass the Hardy retractor, and this incision would then be closed with one or two interrupted 5/0 nylon sutures. The nose was packed bilaterally using saline-soaked 7.5-cm Merocel packs within two fingers of a standard surgical glove, retained in place by a pack secured by ties passed behind the head. Antibiotic prophylaxis was given to all cases for 24 hours post-operatively. Prior to closure (and, where used, insertion of the myofascial graft), meticulous haemostasis would be established within the pituitary fossa, often by packing and gentle irrigation with saline and/or hydrogen peroxide, and always by patient observation. After removing the retractor from the right anterior nares, a Killian’s retractor would be passed into the left side to reposition the septum. In three cases, a small releasing incision was required in the right anterior nares to pass the Hardy retractor, and this incision would then be closed with one or two interrupted 5/0 nylon sutures. The nose was packed bilaterally using saline-soaked 7.5-cm Merocel packs within two fingers of a standard surgical glove, retained in place by a pack secured by ties passed behind the head. Antibiotic prophylaxis was given to all cases for 24 hours post-operatively.

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Epistaxis

There were no cases of significant post-operative epistaxis. Most patients had a light discharge of blood-stained mucus after removal of the nasal packs, but in all cases, this stopped the same day. Seven patients (10%) experienced a discharge sufficient to be documented in the medical records, but no patients had to undergo re-packing of the nose or had frank blood discharging from the nostrils. There were no cases of delayed (secondary) epistaxis during hospital stay nor was it recorded at follow-up.

Septal complications

There were no cases of septal perforation or deformity at 3, 6 and 12 months follow-up. A number of patients, particularly those with acromegaly, reported improvement in their breathing and reduced tendency to snoring after surgery.

Anosmia/hyposmia

Patients were specifically asked about change in their sense of smell and taste. None reported any abnormality immediately after operation and at follow-up.

Other symptoms

One patient developed numbness of the right cheek because of damage to the maxillary division of the trigeminal nerve resulting from inadvertent straying from the correct trajectory in a procedure undertaken by an experienced trainee. This unfortunate complication emphasised the importance of patient observation. After removing the retractor from the right anterior nares, a Killian’s retractor would be passed into the left side to reposition the septum. In three cases, a small releasing incision was required in the right anterior nares to pass the Hardy retractor, and this incision would then be closed with one or two interrupted 5/0 nylon sutures. The nose was packed bilaterally using saline-soaked 7.5-cm Merocel packs within two fingers of a standard surgical glove, retained in place by a pack secured by ties passed behind the head. Antibiotic prophylaxis was given to all cases for 24 hours post-operatively. Prior to closure (and, where used, insertion of the myofascial graft), meticulous haemostasis would be established within the pituitary fossa, often by packing and gentle irrigation with saline and/or hydrogen peroxide, and always by patient observation. After removing the retractor from the right anterior nares, a Killian’s retractor would be passed into the left side to reposition the septum. In three cases, a small releasing incision was required in the right anterior nares to pass the Hardy retractor, and this incision would then be closed with one or two interrupted 5/0 nylon sutures. The nose was packed bilaterally using saline-soaked 7.5-cm Merocel packs within two fingers of a standard surgical glove, retained in place by a pack secured by ties passed behind the head. Antibiotic prophylaxis was given to all cases for 24 hours post-operatively.
of paying careful attention to anatomical landmarks and to the perioperative lateral radiological screening.

One patient had a purulent nasal discharge at outpatient follow-up, which responded to a course of broad spectrum antibiotics prescribed by an ENT surgeon.

There were no complaints of nasal or facial pain resulting from the procedure, and no cases of anosmia. There were no complaints of intraoral pain or numbness. However, there was one death resulting from intrasellar haemorrhage from the internal carotid artery [mortality rate (n = 1/70), 1.4%; overall complication rate (n = 3/70), 4.2%].

### Discussion

The use of the microscope for pituitary surgery has been established as the gold standard for the latter part of the 20th century following the work of Hardy. However, in the 1990s, the use of the endoscope became increasingly prevalent due to the unparalleled view of the surgical field it afforded. There has been a substantial amount of work done recently to compare these two techniques to establish the gold standard.

However, both of these techniques are not without their advantages and disadvantages. Endoscopic pituitary surgery is slowly becoming the procedure of choice because of improved visualisation of the surgical field, reduced length of stay and complications. Microscopic pituitary surgery has the advantage of being easily used by a single surgeon and affords a stereoscopic three-dimensional view. Inevitably, when compared with the endoscopic technique, visualisation of the surgical field as well as manoeuvrability is restricted.

A recent meta-analysis of the endoscopic technique showed it to be a safe and viable procedure when assessing gross tumour removal rates, endocrine function and complication rates. In fact, endocrine outcomes in the short-term have been shown to be better with the endoscopic technique when compared with the microscopic technique. Long-term results for endoscopic surgery, however, are not yet available despite these promising short-term results. For this reason, microscopic pituitary surgery still has an important role to play in this domain.

The major complications for pituitary surgery include CSF leaks, vascular injury, intracranial injury, endocrine abnormalities and infection. Complication rates in both methods have been found to be comparable. Otolaryngologists are becoming increasingly involved in the care of this population of patients because of established familiarity with nasal anatomy and with the endoscope.

In theory, the endoscopic approach has a decreased potential for nasal complications because of limited septal dissection. However, the use of the microscope can be associated with a high incidence of nasal complications depending on the approach used. A literature search revealed that rhinological complications after sublabial trans-septal trans-sphenoidal surgery have ranged as high as 28%–35%. Nasoseptal perforations have been reported in 1%–13% of patients, upper lip anaesthesia in 5%–28% and post-operative anosmia in 5.5%.

A study performed by Marquardt et al. reported post-operative complications of epistaxis (11.5%), facial swelling (9.6%), ecchymotic cheeks (15.4%) and raccoon eyes (3.8%). Watson et al. and Wilson et al. found that the sublabial approach to the sphenoid can cause denervation or pulp death of some of the anterior teeth.

Although endoscopic pituitary surgery is proving to have clear advantages in terms of complications and visualisation over the traditional trans-septal approach and, at least in the short-term, it is proving as effective in tumour removal, however, it has its own disadvantages. Gondim et al. reported reduction of field depth, constant need of manual control of the endoscope and required experience of the endoscope technique. In addition to this, a higher incidence of post-operative CSF leaks is reported. Anatomical variations may also hinder access to the sphenoid sinus. A prospective study of anatomical variations in patients undergoing this procedure found that septal deviation was the most commonly visualised variation. The incidence of this may be 63% in patients with sinonasal symptoms. Nevertheless, a recent meta-analysis by Tabee et al., looking at 9 studies (821 patients), showed gross tumour removal rate and hormone resolution of 78%–84%. Mortality rate was 0.24% (2/821—both because of vascular injury) with a CSF leak rate of 2%.

There has, however, been less comparison in the literature of the sublabial trans-septal trans-sphenoidal approach to the sphenoid compared with the sublabial sublabial approach to the sphenoid.

### Table 1: Total complication rate

<table>
<thead>
<tr>
<th>Complication rates</th>
<th>At 24 months follow-up (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epistaxis</td>
<td>0</td>
</tr>
<tr>
<td>Septal perforation</td>
<td>0</td>
</tr>
<tr>
<td>Anosmia</td>
<td>0</td>
</tr>
<tr>
<td>CSF leak</td>
<td>0</td>
</tr>
<tr>
<td>Meningitis</td>
<td>0</td>
</tr>
<tr>
<td>Purulent nasal discharge</td>
<td>1.4 (n = 1/70) resolved with antibiotics</td>
</tr>
<tr>
<td>Maxillary nerve damage</td>
<td>1.4 (n = 1/70)</td>
</tr>
<tr>
<td>Mortality</td>
<td>1.4 (n = 1/70) internal carotid artery damage</td>
</tr>
</tbody>
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endoscopic endonasal approach with the microscopic endonasal approach to the sella. The first reported method of the direct transnasal approach was by Griffith and Veerapen. Whilst submucous trans-septal approaches to the sphenoid sinus afford the advantage of remaining directly in the midline during the approach to the sella and also confer a slightly better exposure, the reported incidence of nasal complications from such techniques is high.

A literature search revealed that rhinological complications after sublabial trans-septal trans-sphenoidal surgery have ranged as high as 28%–35%. Nasoseptal perforations have been reported in 1%–13% of patients, upper lip anaesthesia in 5%–28% and post-operative anosmia in 5.5%.

The first reported series of the direct transnasal approach was by Griffith and Veerapen, who in a series of 150 patients showed no septal perforations; 2 of 150 patients had secondary epistaxis and both were treated conservatively with no other major rhinological complications. Hyposmia was also noticed in 0.5% of patients. In the aforementioned study, only one patient was admitted for a secondary haemorrhage 10 days post-operatively.

It may be argued that better outcomes are to be expected following surgery that adopts a strictly midline approach, but in our retrospective study of 70 cases, the outcomes compared very favourably with those reported by Ciric et al. For example, we achieved a biochemical cure rate in acromegaly of 75% (9/12 cases) from surgery alone compared with 60% in Ciric’s study, and an almost identical rate of production of hypopituitarism of 19%. Furthermore, a direct transnasal approach is easily adaptable to endoscopic techniques and to image-guided or frameless stereotactic assistance.

A subsequent study of 104 patients using the direct technique done by Cooke and Jones reported no septal, sinus or dental complications, but they had a major complication rate of 5.8%. There followed a series of smaller studies (such as those by Tan and Jones) which reported no septal perforation and only 0.5% of nasal pain, which resolved after 1 week.

To date, the largest series on the endonasal microscopic approach to the sella has been by Fatemi et al. involving 812 patients. Surgical complications included 19 post-operative CSF leaks (2%), 6 post-operative haematomas (0.7%), 4 carotid artery injuries (0.4%), 4 new permanent neurological deficits (0.4%), 3 cases of bacterial meningitis (0.3%) and 2 deaths (0.2%). The overall complication rate was higher in the first 500 cases in the series and in extended approach cases. When we specifically look at nasal complications, the rates were 1% for delayed epistaxis requiring embolisation and 1.5% for delayed sinusitis requiring sinus endoscopy. The authors have chosen not to mention how sinusitis was defined and whether sinus washout or surgery was required. Here the endoscopic assistance was utilised in 163 cases. Our results for nasal complications are extremely favourable when compared with all the aforementioned series. The mortality rate of 1.4% is higher than that in the Fatemi (0.2%) series and in the recent meta-analysis of endoscopic work (0.24%). However, Ciric et al. in a survey concluded that there was significant reduction in the complication rates with increasing experience at thresholds of 200 and 500 cases. Our series only has 70 cases, but it is one of the few studies of pure transnasal microscopic work without the assistance of an endoscope.

In our review of the literature, we found only two other sizable recent series looking at this method of excision with respect to nasal complications reported by Marquardt et al. (104 patients) and Zada et al. (78 patients). The findings of these studies are summarised in Table 2.

Further, subgroup analysis in the series by Zada et al. and Dusick demonstrates that of the subjects who had previously undergone trans-septal surgery, approximately 87% preferred the endonasal microscopic approach.

### Table 2 Summary of nasal complications from endonasal microscopic surgery from previous series in the literature

<table>
<thead>
<tr>
<th>Author</th>
<th>Number of cases</th>
<th>Nasal complications following microscopic endonasal surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatemi et al.</td>
<td>812</td>
<td>Incidence of epistaxis requiring embolisation was 1% and delayed sinusitis requiring sinus endoscopy was 1.5%</td>
</tr>
<tr>
<td>Zada et al.</td>
<td>78</td>
<td>Sinonasal problems</td>
</tr>
<tr>
<td>Marquardt et al.</td>
<td>104</td>
<td>Epistaxis was reported in 1 case</td>
</tr>
<tr>
<td>Cooke et al.</td>
<td>104</td>
<td>Major complication rate of 5.8% with no reported long-term nasal complications</td>
</tr>
</tbody>
</table>

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The advent of the endoscope has heralded a new age in pituitary surgery with extremely promising short-term results. However, microscopic surgery, which has been the gold standard, still has a role to play in this arena. Major complication rates have been shown to be similar for both techniques. Our results, along with those of other series of the endonasal microscopic approach, show that nasal complication rates are low and the perception that this may be further reduced by endoscopic surgery may not be founded.

A full comparative trial of endonasal endoscopic vs endonasal microscopic pituitary surgery is needed, along with the long-term data on endoscopic cure rates. As long as these long-term cure rates are equivalent to microscopic resection, the endoscope is likely to be the preferred instrument of choice. However, the endonasal microscopic method should not be totally forgotten to ensure that the skill of this relatively safe method is not lost.

Conclusion
Our findings add weight to those of other authors that a direct transnasal approach provides safe trans-sphenoidal access to the sella with a very low rate of nasal complications. We would again emphasise the importance of strict adherence to anatomical landmarks and to the role of lateral radiological screening.

1. Nasal complication rates from this method are low.
2. A microscope can be successfully used in an endonasal approach to the sella on its own.
3. It can also be a useful adjunct to the endoscope and this skill set should not be forgotten by ENT surgeons and neurosurgeons.
4. It appears that the method of approaching the sella (transnasal vs trans-septal) rather than the instrument used helps determine the rate of nasal complications. A full comparative trial of both endonasal methods is needed.

Abbreviations list
CSF, cerebrospinal fluid; CT, computed tomography; ENT, ear, nose and throat; MRI, magnetic resonance imaging.

References