Value of endoscopy for maximizing tumor removal in endonasal transsphenoidal pituitary adenoma surgery

Clinical article

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Object. Endoscopy as a visual aid (endoscope assisted) or as the sole visual method (fully endoscopic) is increasingly used in pituitary adenoma surgery. Authors of this study assessed the value of endoscopic visualization for finding and removing residual adenoma after initial microscopic removal.

Methods. Consecutive patients who underwent endoscope-assisted microsurgical removal of pituitary adenoma were included in this study. The utility of the endoscope in finding and removing residual adenoma not visualized by the microscope was noted intraoperatively. After maximal tumor removal under microscopic visualization, surgeries were categorized as to whether additional tumor was removed via endoscopy. Tumor removal and remission rates were also noted. Patients undergoing fully endoscopic tumor removal during this same period were excluded from the study.

Results. Over 3 years, 140 patients (41% women, mean age 50 years) underwent endoscope-assisted adenoma removal of 30 endocrine-active microadenomas and 110 macroadenomas (39 endocrine-active, 71 endocrine-inactive); 16% (23/140) of patients had prior surgery. After initial microscopic removal, endoscopy revealed residual tumor in 40% (56/140) of cases and the additional tumor was removed in 36% (50 cases) of these cases. Endoscopy facilitated additional tumor removal in 54% (36/67) of the adenomas measuring ≥2 cm in diameter and in 19% (14/73) of the adenomas smaller than 2 cm in diameter (p < 0.0001); additional tumor removal was achieved in 20% (6/30) of the microadenomas. Residual tumor was typically removed from the suprasellar extension and folds of the collapsed diaphragma sellae or along or within the medial cavernous sinus. Overall, 91% of endocrine-inactive tumors were gross-totally or near-totally removed, and 70% of endocrine-active adenomas had early remission.

Conclusions. After microscope-based tumor removal, endoscopic visualization led to additional adenoma removal in over one-third of patients. The panoramic visualization of the endoscope appears to facilitate more complete tumor removal than is possible with the microscope alone. These findings further emphasize the utility of endoscopic visualization in pituitary adenoma surgery. Longer follow-ups and additional case series are needed to determine if endoscopic adenomectomy translates into higher long-term remission rates.

Key Words • pituitary adenoma • endonasal • microscope • endoscope • endoscope-assisted surgery • outcome • pituitary surgery

In the late 1960s, Hardy popularized the use of the operating microscope in transsphenoidal surgery for selective adenomectomy. Over the next 3 decades, the microscopic transsphenoidal procedure via a sublabial or direct endonasal approach became the “gold standard” for pituitary tumor removal. An endoscope with an external light source mounted on a rigid shaft was first used for transsphenoidal surgery by Guiot in the early 1960s. Hardy also occasionally used the endoscope to explore the sellar cavity after tumor removal to look for residual tumor. In 1977, Apuzzo and colleagues reported the use of an angled telescope during intrasellar procedures to assist with visualization for tumor removal or gland ablation. In 1992, Jankowski and colleagues first described successful endonasal endoscopic resection of pituitary adenomas in 3 patients. The first clinical series (50 patients) of purely endoscopic pituitary tumor removals without the use of a microscope was documented.
by Jho and Carrau in 1997. Since then, endoscopic pituitary surgery has gained great popularity, and many microscopic pituitary surgeons have transitioned to an endoscope-assisted method or fully endoscopic trans-sphenoidal approach for pituitary adenomas and other parasellar tumors. Over the last decade, many endoscopic pituitary surgeons have transitioned from a single-nostril to a binostril approach given the increased maneuverability and expanded parasellar access. With refinements in endoscope image quality and dedicated instrumentation, endoscopic pituitary tumor removal in experienced hands has now become an excellent alternative to microscopic tumor removal.

The advantage of the endoscope over the microscope in pituitary tumor removal is enhanced visualization. Given that the light source can be taken directly into the sphenoid sinus and sella, the improved panoramic high-resolution view can translate into greater degrees of tumor removal than is possible with the tunnel vision and relatively restricted access of the microscope, illuminating the sellar area through an endonasal or sublabial speculum. To date, there are no randomized prospective trials of purely endoscopic versus microscopic pituitary tumor removal, and many neurosurgeons still perform microscopic pituitary tumor removal without the endoscope or with limited endoscope assistance. A gradual adopter of the fully endoscopic approach, the senior author (D.F.K.) has used an endoscope-assisted method for several years and specifically documented any residual tumor visualized and removed when the endoscope was introduced after initial maximal tumor removal was completed with the microscope. Herein, we assess the value of the endoscope for finding and removing additional adenoma in endonasal pituitary surgery.

Methods

Patient Population and Data Collection

The Saint John’s Health Center institutional review board approved this retrospective study of patient data. The Endonasal Surgery Database was utilized, and patients’ clinic notes, operative notes, imaging studies, and hormonal studies were reviewed; intraoperative observations, surgical complications, and clinical outcomes were documented. Patients were categorized based on tumor type, maximal tumor diameter, presence of cavernous sinus invasion, and prior transsphenoidal surgery.

Between July 2007 and December 2010, 197 consecutive patients underwent either endoscope-assisted or fully endoscopic removal of pituitary adenoma. Of these, 149 patients underwent endoscope-assisted microsurgical removal of a pituitary adenoma by the senior author (D.F.K.). Nine patients initially surgically treated at our institution (D.F.K.) required a reoperation for residual tumor during the study period, but these reoperations were excluded from analysis since we aimed to assess the senior author’s first attempt at tumor resection with the endoscope-assisted microscopic technique. Additionally, 48 patients who underwent a fully endoscopic approach for adenoma removal (during the last 15 months of the study) were excluded from the analysis. Thus, the final study population consisted of 140 patients undergoing their first surgery or reoperation after an initial surgery at another institution. Strict selection criteria for using an endoscope-assisted approach versus a fully endoscopic approach were not used. In general, however, during the later phase of the study period, larger macroadenomas with large suprasellar and/or lateral extensions were routinely removed with a fully endoscopic binostril approach. All procedures were performed by the senior author (D.F.K.) at Saint John’s Health Center.

Perioperative Imaging and Endocrine Evaluation

All patients underwent pituitary MRI with and without gadolinium prior to surgery. Dynamic MRI was performed specifically in the setting of biochemical Cushing disease with no adenoma visualized on conventional pituitary MRI.

Hormonal data included pre- and postoperative levels of serum prolactin, morning serum cortisol and ACTH levels, 24-hour urinary free cortisol levels (for patients with Cushing disease), GH levels, IGF-1 levels, free or bioavailable testosterone levels, thyroxine levels, and TSH levels.

Surgical Technique

A direct endonasal transsphenoidal approach to the sellar region is performed as originally described by Griffith and Veerapen, with several modifications as described below and in our recent publications. Surgical navigation (BrainLab or Stryker) is used in all cases and intermittently throughout the procedure. The initial approach and tumor removal are performed under microscopic visualization through one nostril with a short endonasal trapezoidal speculum of 60 or 70 mm. Given the slightly off-midline trajectory afforded by the endonasal approach, the contralateral nostril is chosen for lesions extending eccentrically to one side. The ipsilateral middle turbinate is out-fractured by the speculum. A wide and tall sphenoidotomy is performed, extending beyond the sphenoid ostia bilaterally and including a partial posterior ethmoidectomy to facilitate use of the endoscope. Once satisfactory exposure is achieved with the microscope, a 0° 4-mm rigid endoscope (Karl Storz) is used to evaluate completeness of soft tissue and bone removal, as well as the extent of dural exposure along the tuberculum sellae for lesions with significant suprasellar extension and along the cavernous sinus for tumors that extend beyond the medial cavernous sinus wall. The Doppler probe is used to confirm the location of the cavernous internal carotid artery.

After creating a wide U-shaped dural opening, tumor excision is performed under microscopic visualization using angled ring curettes and microdissectors to achieve complete removal. For macroadenomas, folds of the collapsed normal gland and diaphragma sella are carefully explored, as are the lateral recesses of the sella and medial cavernous sinus walls. Especially for larger tumors or those with lateral extensions, ring curetting is sometimes performed in “blind” fashion without direct visualization along the medial cavernous sinuses or into diaphragmatic folds.

N. McLaughlin et al.
Value of the endoscope in microscopic endonasal pituitary adenoma

After maximal tumor removal under microscopic visualization, the 0° endoscope followed by the 30° or 45° endoscope is used to assess the completeness of tumor removal by reexploring the entire sellar cavity including the suprasellar areas, the lateral recesses, and along or in the medial cavernous sinuses. Early in this series of patients, the endoscopic part of the case was performed with only a 2-hand technique or with a fixed endoscope holder and speculum in place. In the latter half of the series, a 3-hand technique was typically used, with an assistant driving the endoscope and the speculum removed to facilitate greater maneuverability of the endoscope and other instruments, including straight and curved suction cannulas and ring curettes. Notably, at this point, the nostril of approach is quite expanded and stretched by the force of the speculum even after the instrument’s removal, providing an excellent corridor for endoscopic exploration and tumor removal. Finally, in some of the most recent cases in this series, the approach was converted to a binostril technique after completing a partial posterior septectomy. For all cases, skull base reconstruction proceeds in a tailored fashion depending on the grade of intraoperative cerebrospinal fluid (CSF) leak. Nasal packing is not used.

Outcome Analysis

Each case was categorized based on whether the endoscopic view confirmed complete or incomplete tumor removal. If residual tumor was seen, patients were subcategorized as to whether the residual tumor was removed under endoscopic visualization.

For endocrine-inactive macroadenomas, extent of tumor removal was documented by postoperative MRI 3 months or more after surgery and was categorized as gross total, near total (> 90% volume reduction), or subtotal, with subsequent MRI performed at 6- to 12-month intervals depending on the clinical scenario.

For endocrine-active adenomas, remission criteria were defined as follows. For prolactinomas, tumor remission was defined as an early postoperative random GH level < 2.5 ng/ml and a normal serum prolactin level < 10 ng/dl and a normal serum prolactin level < 20 ng/dl at the last follow-up in the absence of disease.36 In a subset of acromegalic patients, an OGTT was also performed, and the results were used in determining remission status based on a nadir GH level < 0.4 μg/L as a criterion for remission.21,35 For TSH-secreting adenomas, normalization of both TSH and total thyroxine at least 6 months after surgery constituted the remission criterion.

Surgical complications were identified through the operative reports and postoperative clinic notes. Statistical analyses were performed using the Prism 5.0 software (GraphPad Software, Inc.). Percentages of patients between groups were compared using the Fisher exact test. A p < 0.05 was considered significant.

Results

Demographics, Imaging, and Endocrinology Details of the Study Population

The patient population consisted of 140 consecutive patients with a mean age of 50.4 years ± 14.8 years; 41% were women and 59% were men. Among these patients were 23 reoperations (16%) following a prior transsphenoidal surgery performed at another institution. One hundred forty endoscope-assisted adenoma removals were performed for the first time by the senior author (D.F.K.). Overall, 69 patients had an endocrine-active adenoma (39 macroadenomas and 30 microadenomas) and 71 had endocrine-inactive macroadenomas. Among the 69 endocrine-active adenomas, there were 29 prolactinomas, 22 ACTH-secreting adenomas (including 5 with no adenoma seen on MRI), 15 GH-secreting adenomas, and 3 TSH-secreting adenomas. Clinical and imaging evidence of pituitary apoplexy was present in 20.7% (29/140) of patients including 21% (15/71) of those with endocrine-inactive adenomas and 20% (14/69) of those with endocrine-active tumors. Cavernous sinus invasion was visualized on preoperative images and confirmed intraoperatively in 27% (38/140) of patients, including 28% (20/71) of those with nonfunctional adenomas and 26% (18/69) of those with functional tumors. Of the 23 patients undergoing reoperations, 14 had macroadenomas (6 endocrine-active adenomas and 8 endocrine-inactive adenomas) and 9 had microadenomas (all endocrine-active). Among the 110 macroadenomas, 34 (31%) were 10–19 mm in diameter, 67 (61%) were 20–39 mm in diameter and 9 (8%) were giant, that is, ≥ 40 mm in maximal diameter (Table 1).

Intraoperative Findings

After microscopic tumor removal, endoscopic inspection demonstrated residual tumor in 40% (56/140) of patients; additional tumor could be removed in 89% (50/56) of these cases, for a total of 36% (50/140) of patients who benefitted from endoscopic visualization. Additional tumor was removed in 20% (6/30) of microadenoma cases and 40% (44/110) of macroadenoma cases (Table 1). When considering maximal tumor diameter, additional removal was achieved in 54% (36/67) of adenomas 2 cm or larger in diameter and in 19% (14/73) of tumors smaller than 2 cm in diameter (p < 0.0001, Fisher exact test; Fig. 1). Residual tumor seen under direct endoscopic visualization but unobservable with the microscope was typically located in the anterior or posterior superior aspect of the sella/suprasellar space, in the lateral suprasellar recesses, along the medial wall of the cavernous sinuses, or within the medial cavernous sinuses. Among the 38 patients with cavernous sinus invasion, 21 (55%) had additional tumor removed using endoscopic visualization. Among the 6 patients whose residual tumor was seen with the endoscope but not removed, the reason for leaving it was fibrous and rubbery tumor consistency or tumor adherence to the diaphragma sellae, medial cavernous sinus, or carotid artery.
For endocrine-inactive adenomas, residual tumor was viewed in 46% (33/71) of cases and removed using the endoscope in 88% (29/33) of such cases (Table 1). For the endocrine-active adenomas, the endoscope allowed visualization of residual tumor in 33% (23/69) of cases, and the residue was removed in 91% (21/23) of these cases. Among the 6 microadenoma cases in which residual tumor was removed, cavernous sinus invasion was found in 2 patients.

Tumor Removal and Remission Rates

The median clinical follow-up was 17 months, ranging from 3 to 46 months, and the median radiological follow-up was 15 months, ranging from 3 to 46 months. Early remission was achieved in 70% (48/69) of endocrine-active adenomas according to standard early remission criteria.\(^2,18,21,35,36,45,46\) Specifically, remission was achieved in 62% (18/29) of patients with a prolactinoma and in 73% (16/22) of those with Cushing disease. Early remission was achieved in 73% (11/15) of patients with acromegaly; among these 11 were 5 with an OGTT confirming the remission status. All 3 patients with TSH-secreting adenomas had early remission. Of the 11 patients with prolactinomas who did not have a remission, the average preoperative prolactin level was 1499 ng/dl (range 146–5822 ng/dl); 10 of these 11 patients had tumors 2 cm or larger in diameter, 5 had cavernous sinus invasion, 8 had apoplexy, and 1 had undergone prior surgery. Of the 6 patients with Cushing disease without remission, all had at least 1 of the following: nonvisible adenoma (4), cavernous sinus invasion (1), or prior surgery (3). Of the 4 patients with acromegaly without remission, all had cavernous sinus invasion and 2 had undergone prior surgery. In comparing patients with endocrine-active adenomas who had no cavernous sinus invasion or prior surgery with those who had both or either, remission rates were 79% (33/42) versus 56% (15/27; p = 0.11, Fisher exact test; Table 2). Of the 69 patients with endocrine-active tumors, early remission was achieved in 67% (41/61) of patients with endoscopically visualized and resected residual tumor versus 71% (34/48) of those with no residual tumor seen and/or resected (p = 0.8, Fisher exact test).

Resection status was assessed at the 3-month or later MRI follow-up in 67 of the 71 patients with endocrine-inactive macroadenomas; 4 patients did not have 3-month or later imaging follow-up. Gross-total resection and NTR were respectively achieved in 79% and 12% of endocrine-inactive macroadenomas based on 3-month or later MRI, for a total of 91% (61/67) of patients with GTR or NTR. The mean maximal tumor diameter was 23 mm ± 9 mm in the 53 patients with GTR versus 30 mm ± 8 mm in the 14 patients with NTR or STR (p = 0.015, t-test). In comparing patients with endocrine-inactive adenomas who had no cavernous sinus invasion or prior surgery versus those who had both or either, GTR was achieved in 88% (38/43) vs 62% (15/24; p = 0.02, Fisher exact test; Table 3). Of the endocrine-inactive adenomas with STR (6), 100% had a maximal tumor diameter ≥ 2 cm, 67% had cavernous sinus invasion, and 33% had apoplexy. Considering the 67 patients with endocrine-inactive tumors with 3 months’ or more follow-up, GTR was achieved in 62% (18/29) of patients in whom residual tumor was endoscopically visualized and removed versus 92% (35/38) of those in whom no additional tumor was visualized and/or resected (p = 0.005, Fisher exact test). However, endocrine-inactive tumors in which no residue was endoscopically removed were on av-

![Table 1: Intraoperative endoscopic findings as regards endocrine status and tumor size](image)

<table>
<thead>
<tr>
<th>Category</th>
<th>Total No. of Adenomas</th>
<th>No Additional Tumor Removed</th>
<th>Additional Tumor Seen &amp; Removed</th>
<th>Additional Tumor Seen But Not Removed</th>
</tr>
</thead>
<tbody>
<tr>
<td>tumor endocrine status</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>endocrine-inactive</td>
<td>71</td>
<td>38 (54)</td>
<td>29 (41)</td>
<td>4 (5)</td>
</tr>
<tr>
<td>endocrine-active</td>
<td>69</td>
<td>46 (67)</td>
<td>21 (30)</td>
<td>2 (3)</td>
</tr>
<tr>
<td>tumor size</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>microadenoma</td>
<td>30</td>
<td>24 (80)</td>
<td>6 (20)</td>
<td>0</td>
</tr>
<tr>
<td>macroadenoma</td>
<td>110</td>
<td>60 (55)</td>
<td>44 (40)</td>
<td>6 (5)</td>
</tr>
</tbody>
</table>

![Fig. 1. Bar graph showing the number of adenoma cases (y axis) with additional tumor removed in relation to tumor size. Light gray bars represent total adenomas; dark gray bars, adenomas with additional tumor removed.](image)
Value of the endoscope in microscopic endonasal pituitary adenoma

TABLE 2: Endocrine-active adenomas: early remission rate related to cavernous sinus invasion and prior surgery

<table>
<thead>
<tr>
<th>Factor</th>
<th>Cavernous Sinus Invasion Only</th>
<th>Reop Only</th>
<th>Cavernous Sinus Invasion &amp; Reop</th>
<th>No Cavernous Sinus Invasion or Reop</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>no. of patients</td>
<td>12</td>
<td>12</td>
<td>3</td>
<td>42</td>
<td>69</td>
</tr>
<tr>
<td>remission rate (no. of patients [%])</td>
<td>8 (67)</td>
<td>7 (58)</td>
<td>0 (0)</td>
<td>33 (78)</td>
<td>48 (70)</td>
</tr>
</tbody>
</table>

Surgical Complications

In this series, no permanent cranial neuropathies, visual deterioration, or postoperative hematomas developed. One postoperative CSF leak occurred early in the series and was successfully treated with a lumbar drain. There was 1 death: an 85-year-old man with a giant 4-cm adenoma who presented with complete loss of vision, severe apoplexy, and diffuse subarachnoid hemorrhage on head CT and brain MRI. Endonasal tumor removal was uneventful, and no CSF leak occurred intraoperatively. His initial postoperative head CT showed no pneumocephalus or hemorrhage progression; however, within 12 hours of surgery, his level of consciousness deteriorated and the family requested comfort measures.

Discussion

Summary of Findings

In this series of 140 patients undergoing microscopic endonasal maximal tumor removal, residual tumor was endoscopically identified and removed in 36% of cases including 54% of patients with adenomas 2 cm or larger and in 19% with adenomas smaller than 2 cm. Patients with cavernous sinus invasion also had residual tumor removed under endoscopic visualization in 57% of cases. Overall, gross-total or near-total removal was achieved in 91% of endocrine-inactive macroadenomas and early remission was achieved in 70% of endocrine-active adenomas.

Comparison of Fully Endoscopic Versus Microscopic Pituitary Adenoma Removal

Over the past decade, the endonasal endoscopic technique for removal of pituitary adenomas and other parasellar tumors has gained wider acceptance in the neurosurgical community. Numerous single-institution studies and several meta-analyses have compared the fully endoscopic approach with the microscopic technique for pituitary tumor removal. Overall, these studies have generally shown that the fully endoscopic approach is at least as safe as the microsurgical approach. While the efficacy of the fully endoscopic approach as regards long-term remission rates for functional adenomas and gland recovery remains under evaluation, there is growing evidence that the procedure, particularly for larger adenomas, leads to incrementally greater degrees of adenoma removal than a purely microscopic technique.

For example, Messerer et al. recently compared 2 consecutive groups of 82 patients with endocrine inactive adenomas who underwent fully endonasal endoscopic removal or sublabial microscopic removal. Gross-total removal was significantly higher (74% vs 56%) in the endoscopic removal group, and the disparity between the 2 groups was even higher with larger macroadenomas. Similarly, Enseñat et al. compared outcomes in 25 patients undergoing endonasal endoscopic adenoma removal with those in 23 patients undergoing sublabial microscopic removal. Gross-total removal was significantly higher (60% vs 35%) in the endoscopic group. Other recent comparison studies have shown similar trends of greater degrees of tumor removal using endoscopy.

Regarding functional adenomas, there is early evidence that endoscope may yield higher remission rates in select patients, but well-controlled comparison studies are lacking. For example, in 60 patients with acromegaly treated with a fully endoscopic approach, Jane et al. achieved remission in 100% of patients with microadenomas and in 61% of those with macroadenomas. Notably, remission rates in patients with invasive tumors had low remission rates, similar to rates in microscopic surgical series.

Endoscope-Assisted Removal and the Future of Microscopic Removal of Adenomas

The major question addressed here is, does the en-
Dorsoscopic view facilitate additional tumor removal after maximal microscopic removal? Our results strongly indicate yes and reinforce findings by others who have compared these 2 visualization modalities in distinct patient series, as noted above. Somewhat surprisingly, a benefit was even shown in a small subset of patients with microadenomas. However, the major patient group that benefits from endoscopy appears to be that with larger macroadenomas and adenomas that invade the cavernous sinuses. Yet, as many studies have shown, even with endoscopy complete removal of invasive adenomas that extend into the cavernous sinus remains an elusive goal, especially for functional adenomas.

Nonetheless, greater degrees of tumor removal in the cavernous sinus may ultimately translate into better disease control, for example, in patients with acromegaly who may have a higher likelihood of remission with medical therapy. Similarly, in patients with nonfunctional adenomas, greater degrees of cavernous sinus tumor removal may delay the need for radiosurgery or stereotactic radiotherapy.

If one accepts the basic tenet that endoscopy allows greater degrees of tumor removal for most patients with macroadenomas and a smaller subset of patients with microadenomas, the next logical question is, what then is the future of the microscope in transsphenoidal surgery? Depending on who is asked, the answers are wide ranging. Most neurosurgeons who have a limited microscopic transsphenoidal experience and have embraced the fully endoscopic approach cannot conceive of going back to the microscope, because in their view the results are simply better given the greatly enhanced visualization. Likewise, our ear, nose, and throat colleagues, who had been performing sinus endoscopy for years before joining neurosurgeons in removing pituitary and parasellar tumors, are also fully convinced that endoscopic tumor removal is the only logical approach. Other neurosurgeons, particularly those with extensive microscopic surgical experience, tend to view the endoscope as a critical tool but not necessarily ideal for every case. As Dr. Oldfield recently noted in an editorial, “It is clear from our experience that larger suprasellar tumors and tumors extending laterally beyond the direct view of the operating microscope are often best addressed with the endoscope, whether endoscopic surgery alone or endoscope assisted, whereas the very small tumors, those occurring with some frequency in Cushing’s disease, may be best addressed with the operating microscope. Tumors between these extremes—most pituitary tumors requiring surgery—can be addressed via either approach with the expectation of success in most patients.”

A recent article, Zada et al. described a subset of patients (18% of 148 cases) in whom they converted from an endoscopic to a microscopic approach for a variety of intraoperative conditions including altered anatomy from prior surgery, bleeding, Cushing disease, or acromegaly. They emphasized the need for neurosurgeons to be facile and familiar with both microscopic and endoscopic approaches.

As a gradual adopter of endoscopy, the senior author (D.F.K.) has become increasingly convinced of its essential role in transsphenoidal surgery but has not abandoned the microscope. In our overall direct endonasal experience in over 1400 operations beginning in 1998, we have used endoscopy in more than 600 cases, including all those performed since July 2007. For pituitary adenoma surgery, the added value of endoscopy appears to be particularly relevant in exploring the collapsed diaphragmatic folds after initial removal of a large macroadenoma where thin seams of residual tumor can hide, and in visualizing residual tumor along or in the medial cavernous sinus. However, even in smaller tumors, the up-close view allows one to see small fragments of tumor still adherent to the normal gland that are sometimes not seen with the microscope. We believe our findings provide further impetus and rationale for endoscope-assisted or fully endoscopic pituitary adenoma removal.

As for the approach to the sella and initial tumor removal, whether done via a microscopic speculum-based endonasal approach or an endoscopic binostril method, there is probably little difference except that in performing the latter approach, additional soft tissue and bone removal is essential to adequately maneuver the endoscope. For smaller, noninvasive intrasellar adenomas that are easily exposed through the direct view of the microscope, there may be no clear benefits of a fully endoscopic approach over a microscopic approach with endoscopic inspection after maximal tumor removal. For larger tumors, however, especially those with lateral extensions beyond the line of sight of the microscope, a binostril technique is recommended to allow full maneuverability of 2 instruments along with the endoscope. If the initial approach and tumor removal are performed with the microscope, the maximal benefit of endoscopy can be gained by speculum removal, opening of the other nostril, and performing a generous posterior septectomy.

Based on our experience over the past several years and especially the past 2 years working in collaboration with Drs. Amin Kassam and Ricardo Carrau, we strongly advocate performing all pituitary surgeries with endoscopy. We currently use a binostril fully endoscopic approach in over 90% of our pituitary adenoma cases and in all extended parasellar skull base cases. The endoscope-assisted approach is now generally reserved for the occasional microadenoma as well as some smaller macroadenomas and Rathke cleft cysts. In our hands, however, the advantage of the direct endonasal route with endoscopic assistance is the speed of the approach, reduced blood loss, greater preservation of sinonasal anatomy, and simpler postoperative care without the need for multiple postoperative endonasal debridements, which are typically required with the fully endoscopic approach.

**Study Limitations**

We planned to use the endoscope in every case, and one could argue that this knowledge made for a less intense effort to remove challenging or hard-to-see tumor remnants during microscopic visualization. This factor would tend to make the results of additional tumor removal with endoscopic visualization even more favorable. This criticism is similar to one leveled against intraoperative MRI for finding and allowing the removal of additional tumor. Another flaw with our study design is that during the last 15 months of the study period, the senior author (D.F.K.) was also performing fully...
Value of the endoscope in microscopic endonasal pituitary adenoma

dendoscopic tumor removal on many pituitary adenomas and other parasellar tumors. As noted in *Methods*, the selection criteria for an endoscope-assisted versus fully endoscopic tumor removal during this period were not rigorously controlled. Moreover, regarding remission criteria for patients with acromegaly, an OGTT was used in only 5 of 11 patients classified as being in early remission based on an immediate early postoperative GH level and a subsequent normal age- and sex-adjusted IGF-1 level. This lack of data is suboptimal. On the other hand, according to a recent consensus statement, the control of acromegaly is ideally defined by a random GH level < 1 µg/L, a nadir GH level < 0.4 µg/L after an OGTT, and an age- and sex-normalized IGF-1 level. However, no definitive data support the superiority of 1 criterion over the other.21,35 Finally, the duration of follow-up in this series is relatively short. These critiques aside, the major finding of this study remains: endoscopy allows more extensive tumor removal in a large percentage of patients with pituitary adenomas.

Conclusions

The use of endoscopy allowed additional adenoma removal in 36% of patients undergoing an initial microscopic, speculum-based endonasal tumor removal. Further tumor resection was achieved most often in tumors 2 cm or larger in diameter and in those with cavernous sinus invasion; however, 1 in 5 patients with tumors smaller than 2 cm also benefitted from endoscopic visualization. The panoramic visualization and magnification of the endoscope appear to facilitate more complete tumor removal and could translate into higher remission rates for both endocrine-active and endocrine-inactive adenomas. In light of these results and the growing experience of others, we suggest performing pituitary surgery with endoscopic assistance or as a fully endoscopic procedure for both microadenomas and macroadenomas.

Disclosure

Dr. Kelly receives royalties from Mizuho.

Author contributions to the study and manuscript preparation include the following. Conception and design: Kelly, McLaughlin. Acquisition of data: McLaughlin, Eisenberg, Chaloner. Analysis and interpretation of data: Kelly, McLaughlin, Cohan. Drafting the article: McLaughlin. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Kelly. Statistical analysis: McLaughlin. Administrative/technical/material support: Eisenberg, Chaloner. Study supervision: Kelly.

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