Surgical complications associated with the endoscopic endonasal transsphenoidal approach for pituitary adenomas

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Object. To assess postoperative complications related to the surgical procedure, a retrospective analysis was conducted in a series of 146 consecutively treated patients who underwent an endoscopic endonasal transsphenoidal approach to the sellar region for resection of pituitary adenomas between January 1997 and July 2001.

Methods. Complications were divided into groups (nasofacial, sphenoid sinus, sella turcica, supra or parasellar, and endocrine complications) according to the anatomical structures and the systems involved. Overall, a decreased incidence of complications has been observed, compared with large historical series of the traditional microsurgical transsphenoidal approach, likely because of the overview inside the anatomy facilitated by the endoscope, and the decreased surgical trauma.

Conclusions. Transsphenoidal surgery, either microscopic or endoscopic, is a safe procedure in experienced hands, but serious complications still occur and must be reduced as much as possible. Additional improvement can be expected with greater experience and new technical developments. A coordinated team effort with other dedicated colleagues from different specialties is advised.

Key Words • complication • endoscopy • pituitary adenoma • transsphenoidal surgery

The nature of complications associated with transsphenoidal surgery will continue to change as the approach is utilized for the treatment of new conditions, and it is our hope that in the future this procedure may be applied even more effectively and with greater safety than it is at present. From this concluding sentence of the article by Laws and Kern,32 our analysis begins; we have investigated the complications resulting from the endoscopic transsphenoidal procedure that we have been routinely using since 1997.8

After the recent experience with endoscopic transsphenoidal surgery, the procedure is gaining wide acceptance, and its results are beginning to be analyzed by the first groups who performed such approaches.16,25–27 In this report we emphasize the potential for a decrease in the incidence and severity of surgical complications related to the endoscopic procedure compared with the microsurgical approach, which makes the operation attractive for both patients and surgeons.

Clinical Material and Methods

Patient Population

We analyzed 146 consecutive patients who underwent endoscopic endonasal transsphenoidal surgery for treatment of pituitary adenomas; 78 patients were women and 68 were men, and their mean age was 46.06 years (range 16–74 years). The majority (125 individuals) had a pituitary macroadenoma, whereas 21 harbored a microadenoma.

The operations were performed by one of the authors (either P.C. or E.d.D.) at the Department of Neurosurgery of the Federico II University in Naples between January 1997 and July 2001. We used the endoscopic endonasal unilateral approach to the sella, which was performed via an anterior sphenoidotomy, through the existing sphenoid ostium, without the use of a transsphenoidal retractor or any postoperative nasal packing, and with a rigid diagnostic endoscope as the sole visualizing tool.9,25,28 Records of all complications were kept by the junior author (L.M.C.), with the duration of follow up ranging from 3 months to 4 years after the procedure.

Complications were divided into groups according to the anatomical structures and the systems that may be involved. Apart from the anesthetic-related complications associated with the transsphenoidal approach (usually deep vein thrombosis and pulmonary emboli), which are relatively rare,34 we have defined the following categories: 1) nasofacial (that is, approach complications); 2) sphenoid sinus; 3) sella turcica; 4) suprasellar (which include CNS injury and visual complications); 5) parasellar (which include CA and CS cranial nerve complications); and 6) endocrine complications.

Results

The case distribution and the extent of tumor removal are shown in Table 1. Analysis of the results and outcome in these patients is far beyond the scope of this study. Never-
theless, the results of treatment can be derived from Tables 1 through 3, and a list of the general principles we adopted can be found at the beginning of the Discussion section. To-
total, subtotal (>/H11022 80%), and partial removal of nonfunction-
ing adenomas was judged on MR images of the sella ob-
tained before and after intravenous contrast administration,
at least 3 months postsurgery. For secreting adenomas the
results of neuroimaging are completed by the specific blood
assays: where total removal is reported, chemical cure has
also been achieved, but control of the disease was some-
times obtained also after incomplete removal, by using ad-
juvant pharmacological or other therapies.

In secreting adenomas the criteria of cure are considered
to be a fasting random GH level of 2.5 ng/ml, a GH nadir
of 1 ng/ml after an oral glucose tolerance test, and an insu-
lin-like growth factor–I level that is normal for the patient’s
age in GH-secreting tumors; a PRL level of 25 ng/ml or less
in women and 15 ng/ml or less in men and a recovery of
gonadal function (menses in women and sexual function in
men, and/or fertility in both) in PRL-secreting adenomas;
and an ACTH level of 10 to 90 pg/ml, a blood serum cor-
tisol level of 50 to 250 ng/ml in the morning and less than
50 ng/ml in the evening, with a normalization of urinary
cortisol levels (35–135 /H9262 g/24 hours) in ACTH-secreting
tumors.

In macroadenomas, gross total removal was achieved in
45 of 80 nonfunctioning, in 21 of 34 GH- or mixed GH-se-
creting, in four of seven PRL-secreting, and in three of four
ACTH-secreting tumors.

In microadenomas, gross-total removal was achieved in
five of six GH-secreting, in all six PRL-secreting, and in
seven of nine ACTH-secreting tumors (Table 1). Additional
information about the results can be found in our previous
report.16

The complications associated with our procedures are re-
ported according to the aforementioned categories (Table 4)
and are detailed herewith.

**Nasofacial Complications**

Ten days postsurgery, one patient with a GH-PRL–se-
creting macroadenoma suffered delayed bleeding from a
small branch of the sphenopalatine artery, which required
posterior nasal tamponade and subsequent coagulation. One
patient with a GH-secreting macroadenoma presented with
minor nasal bleeding 2 days postsurgery, arising from a sep-
tal vessel, which required 2-day unilateral nasal packing.

**Sphenoid Sinus Complications**

In three patients postoperative sphenoid sinusitis devel-
oped. One of them had a GH-secreting macroadenoma, and
complained of a continual frontal headache 2 months post-
surgery. Sellar MR imaging demonstrated the presence
of sphenoid sinusitis, which was cured with medical treat-
ment. The other two patients had asymptomatic sphenoid
sinusitis that was diagnosed on a sellar MR image obtained
3 months postoperatively. Both patients had been treated
for an intrasellar–suprasellar nonfunctioning macroadeno-
ma, and the sphenoid sinusitis was successfully treated with
medical therapy in both cases.

**Sella Turcica Complications**

In three patients postoperative CSF leak occurred. The
first patient had an intrasellar–suprasellar and right parase-
llar nonfunctioning macroadenoma and returned to our care
15 days postsurgery after the onset of a low-volume CSF
leak, which resolved after a 3-day lumbar drainage. The
other two patients had intrasellar–suprasellar nonfunction-
ing macroadenomas, and in both cases the CSF leak oc-
curred the day after surgery; early reoperation and closure
of the sella with the usual procedure, an intradural–extra-
dural repair with a polyester–silicone dural substitute, and
fibrin glue,12 was successful without the application of lum-
bar drainage.

<table>
<thead>
<tr>
<th>TABLE 1</th>
<th>Tumor type and extent of removal in 146 patients with pituitary adenomas*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lesion</td>
<td>No. of Patients</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>nonfunctioning macro</td>
<td>80</td>
</tr>
<tr>
<td>PRL-secreting macro</td>
<td>7</td>
</tr>
<tr>
<td>micro</td>
<td>6</td>
</tr>
<tr>
<td>GH-secreting macro</td>
<td>30</td>
</tr>
<tr>
<td>micro</td>
<td>6</td>
</tr>
<tr>
<td>ACTH-secreting macro</td>
<td>4</td>
</tr>
<tr>
<td>micro</td>
<td>9</td>
</tr>
<tr>
<td>GH-PRL–secreting macro</td>
<td>3</td>
</tr>
<tr>
<td>GH-TSH–secreting macro</td>
<td>1</td>
</tr>
<tr>
<td>total</td>
<td>146</td>
</tr>
</tbody>
</table>

* Macro = macroadenoma; micro = microadenoma; TSH = thyroid-stimulating hormone.

<table>
<thead>
<tr>
<th>TABLE 2</th>
<th>Patients who had previously undergone a microsurgical transsphenoidal approach for pituitary adenoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrent Tumor</td>
<td>No. of Patients</td>
</tr>
<tr>
<td>nonfunctioning (macro)</td>
<td>14</td>
</tr>
<tr>
<td>GH-secreting (macro)</td>
<td>3</td>
</tr>
<tr>
<td>GH-PRL–secreting (macro)</td>
<td>1</td>
</tr>
<tr>
<td>ACTH-secreting (macro)</td>
<td>2</td>
</tr>
<tr>
<td>total</td>
<td>20</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>TABLE 3</th>
<th>Patients with CS invasion of pituitary adenomas</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lesion</td>
<td>No. of Patients</td>
</tr>
<tr>
<td>nonfunctioning</td>
<td>19</td>
</tr>
<tr>
<td>GH-secreting</td>
<td>9</td>
</tr>
<tr>
<td>PRL-secreting</td>
<td>4</td>
</tr>
<tr>
<td>GH-PRL–secreting</td>
<td>1</td>
</tr>
<tr>
<td>ACTH-secreting</td>
<td>1</td>
</tr>
<tr>
<td>total</td>
<td>34</td>
</tr>
</tbody>
</table>
Complications of endoscopic transsphenoidal surgery

Suprasellar Complications

In one patient with a paninvasive nonfunctioning macroadenoma, only partial removal of the lesion was performed. During the postoperative course, this patient showed a dramatic worsening of consciousness and became comatose. A computerized tomography scan revealed swelling of the residual lesion with compression of the third ventricle and the brainstem; the patient died several days later.

One patient with an intrasellar–suprasellar and bilateral parasellar PRL-secreting macroadenoma presented 4 days postsurgery with headache, stiff neck, fever, and right sixth and seventh cranial nerve palsy. A spinal tap yielded cloudy CSF that grew *Staphylococcus epidermidis* in culture; the meningitis responded to antibiotic treatment and the patient experienced complete recovery from his neurological deficits within 20 days.

An intrasellar–suprasellar hematoma occurred 2 days postsurgery in a patient with an intrasellar–suprasellar nonfunctioning macroadenoma that had been partially removed; this patient had received anticoagulating agents for a previous myocardial infarction. He presented with rapidly progressive worsening of vision, and neuroimaging revealed the presence of a hematoma, which was evacuated transsphenoidally without sequelae and with rapid recovery of vision.

Parasellar Complications

In one patient, major bleeding occurred intraoperatively due to an intracavernous CA injury during the removal of a recurrent intrasellar–parasellar GH-secreting macroadenoma. The bleeding was controlled intraoperatively with tamponade. A pseudoaneurysm of the intracavernous internal CA then developed, which was successfully treated endovascularly by using Guglielmi detachable coils. One patient with an intrasellar GH-secreting microadenoma suffered a transient postoperative sixth nerve palsy, which resolved within 8 weeks.

Endocrine Complications

We did not include among the complications listed in Table 4 the persistence of hormonal hyperactivity in patients with GH-, PRL-, and ACTH-secreting adenomas, because we consider it a result of treatment, not a complication of it; posterior and anterior pituitary insufficiency can be analyzed separately (Table 5).

**Posterior Pituitary Insufficiency.** Diabetes insipidus occurred during the postoperative course in 13 patients: in eight it was temporary, whereas in five it persisted and required vasopressin therapy. In the latter group (with permanent diabetes insipidus), all patients were women whose ages ranged between 21 and 53 years (mean 32.4 years); three had intrasellar nonfunctioning macroadenomas, one had an intrasellar–suprasellar nonfunctioning macroadenoma, and one had an intrasellar–suprasellar PRL-secreting macroadenoma. In four cases total removal of the lesion was achieved, whereas in one patient, who had an intrasellar nonfunctioning macroadenoma, a subtotal removal of the lesion was performed.

**Anterior Pituitary Insufficiency.** In 13.6% of cases, new anterior pituitary insufficiency was detected during the postoperative endocrine evaluation. A deficit in one pituitary axis was found before surgery in 35 patients, in two axes in 21 patients, and in three or more in 24 patients. Worsening of pituitary function after surgery was detected in 20 patients (13.6%), and involved one axis only in 15 cases and two axes in five.

Discussion

It is not our goal in this report to focus on the results of the endoscopic transsphenoidal approach because many more factors, such as the number of giant and invasive adenomas, should be included to derive correct judgments. Nevertheless, the following aspects must be considered in this series of unselected consecutive patients.

**TABLE 4**

Surgical complications in a series of 146 patients with pituitary adenomas*

<table>
<thead>
<tr>
<th>Complication Category</th>
<th>Type of Complication</th>
<th>Patient Age (yrs), Sex</th>
<th>Lesion Type</th>
<th>Time Postop</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>nasofacial epistaxis</td>
<td>IS GH-PRL–secr macro</td>
<td>67, F</td>
<td>10 days</td>
<td>surgery</td>
<td></td>
</tr>
<tr>
<td>epistaxis</td>
<td>IS intra rt para GH-secr micro</td>
<td>54, F</td>
<td>2 days</td>
<td>medical</td>
<td></td>
</tr>
<tr>
<td>sphenoid sinus</td>
<td>sphenoid sinusitis</td>
<td>59, F</td>
<td>intra rt para GH-secr micro</td>
<td>2 mos</td>
<td>medical</td>
</tr>
<tr>
<td>sphenoid sinusis</td>
<td>IS NF macro</td>
<td>40, F</td>
<td>Is NF macro</td>
<td>3 mos</td>
<td>medical</td>
</tr>
<tr>
<td>sphenoid sinusis</td>
<td>IS NF macro</td>
<td>67, F</td>
<td>3 mos</td>
<td>medical</td>
<td></td>
</tr>
<tr>
<td>sella turcica</td>
<td>CSF leakage</td>
<td>52, F</td>
<td>IS rt para NF macro</td>
<td>15 days</td>
<td>lumbar drainage</td>
</tr>
<tr>
<td>CSF leakage</td>
<td>IS NF macro</td>
<td>43, M</td>
<td>1 day</td>
<td>surgery</td>
<td></td>
</tr>
<tr>
<td>CSF leakage</td>
<td>IS NF macro</td>
<td>36, F</td>
<td>1 day</td>
<td>surgery</td>
<td></td>
</tr>
<tr>
<td>supra- &amp; parasellar</td>
<td>swelling of residual lesion</td>
<td>55, F</td>
<td>1 day</td>
<td>medical</td>
<td></td>
</tr>
<tr>
<td>CNS injury</td>
<td>IS NF macro</td>
<td>59, M</td>
<td>4 days</td>
<td>medical</td>
<td></td>
</tr>
<tr>
<td>visual</td>
<td>IS NF macro</td>
<td>59, F</td>
<td>2 days</td>
<td>surgery</td>
<td></td>
</tr>
<tr>
<td>visual</td>
<td>IS NF macro</td>
<td>59, F</td>
<td>2 days</td>
<td>surgery</td>
<td></td>
</tr>
<tr>
<td>CA</td>
<td>ICA injury; pseudoaneurysm</td>
<td>22, F</td>
<td>intra rt para GH-secr macro (rec)</td>
<td>intraop</td>
<td>GDC embolization</td>
</tr>
<tr>
<td>CS, CN</td>
<td>transient VIth CN palsy</td>
<td>43, M</td>
<td>intra GH-secr micro</td>
<td>immediately postop</td>
<td>medical</td>
</tr>
</tbody>
</table>

* CN = cranial nerve; GDC = Guglielmi detachable coil; ICA = internal CA; intra = intrasellar; IS = intrasellar–suprasellar; NF = nonfunctioning; para = parasellar; rec = recurrent; secr = secreting.
Endoscopic endonasal pituitary surgery differs from transsphenoidal microsurgery in the following ways: in the different viewing instruments that are used for the operation, that is, the microscope or the endoscope, with three-dimensional vision offered by the former and with wider and close-up vision permitted by the latter; in that no nasal speculum is used in the pure endoscopic procedure; and in that the endoscopic approach is endonasal, whereas the microsurgical one is often transnasal.

Traditional transsphenoidal surgery has proved to be a reasonably safe procedure in experienced hands. Although the mortality rate is low, usually below 1%,3,13,32,40,43 morbidity is not negligible and complications still occur. Serious and potentially fatal complications must be reduced as much as possible, although it is not possible to eliminate them completely, because of the size and relationship of some lesions to the surrounding structures.

In 1997 Ciric, et al.,13 presented the results of a survey of American neurosurgeons, with a review of the literature and the authors’ personal experience; they reported on the complications of transsphenoidal surgery from their analysis of the data submitted by 958 neurosurgeons who responded to a detailed questionnaire. They assigned each respondent to one of three groups based on the number of transsphenoidal operations performed (< 200, 200–500, > 500), and the results show a decreased percentage of operations resulting in complications with increased experience. We have used the aforementioned work as a basic reference point because of its large number of cases and its recent publication date.

The following is a comparative analysis of the various categories of complications, which correspond to the items in the earlier report on the microsurgical operation.

### Approach Complications

These complications consist of anesthesia of the upper lip and the anterior maxillary teeth; saddlenose; nasal septal perforations (0.3–3%);18,36,42 anosmia caused by undue superior nasal septum dissection;29 diastasis of the maxilla or fracture of the hard palate;33,39 caused by overspreading of the sphenoid; fracture of the orbit;13,32,33 injury or fracture of the cribiform plate and subsequent CSF leak; and bleeding from the mucosal branch of the sphenopalatine artery.3,14,42 None of these was encountered in the analysis of our cases, except for two cases of bleeding from the mucosal branch of the sphenopalatine artery, both in GH-secreting tumors, and with a lower incidence compared with that found in the study of Ciric, et al.13 (Table 6). This can be explained by the fact that the approach does not pass through the mouth, and it could easily be said that the operation starts in the sphenoid sinus when the sphenoid ostium is crossed.

### Sphenoid Sinus Complications

Of the sphenoid sinus complications usually reported (that is, mucocele,3,32,33 a rare and usually late-onset disorder caused by obstruction of air flow at the osteomental complex; fracture of the sphenoid body with injury to the optic nerves and the CAs sometimes due to very thin or absent bone;29 and sinusitis), only sinusitis occurred in our patient series: of three patients, one was symptomatic and two had no symptoms; all were cured with medical treatment. This incidence (2.05%) is lower than that in most reports of com-
Complications of endoscopic transsphenoidal surgery

plications of the microscopic transsphenoidal operation (1–
4% 
and the survey of Ciric, et al. 
( Table 6). The rea
son for the decrease of such complications, and of sinusitis
in particular, is the wide opening of the sphenoid ostium ar
ea, with respect to the osteomeatal complex, without using
a transsphenoidal retractor.

Sella Turcica Complications

With regard to sella turcica complications (that is, sub-
arachnoid hemorrhage, vasospasm, tension pneumocephalus
, and CSF leakage), the only one that occurred was CSF leakage due to breaching of the arachnoid mem
brane, and it was successfully treated in 2.05% of our cases,
as described in detail earlier. This percentage is lower than
the usual rate of occurrence during the traditional transsphenoi
dal approach. 

Suprasellar and Parasellar Complications

A wide range of supr- and parasellar complications was en
countered in our series, because the anatomical, physi
ological, and biological features of the lesions treated us
ing the endoscopic procedure are obviously the same as
those treated using the traditional approach. Analysis of our
data, and its comparison with the relevant literature, reveals
one case of coma, in which the patient died; one case of
meningitis, in which the patient fully recovered; one visual
complication relieved by immediate reoperation; one case
of CA injury in a patient with a recurrent GH-secreting tu
mor, and one transient sixth cranial nerve palsy. Furthermore,
four of five of these kinds of major complications occurred in the first 2 years of experience with the new
endoscopic technique. Nevertheless, all these complications are present at a higher percentage among patients whose
neurosurgeons had performed fewer than 500 microsurgical
transsphenoidal operations ( Table 6).

Endocrine Complications

The endocrine complications are the ones most frequent
ly found after a transsphenoidal procedure, and if we ana
lyze both posterior and anterior pituitary insufficiency,
together, there is some decrease in the incidence of both, when
compared with the larger historical experience with the new
endoscopic technique. Nevertheless, all these complications are present at a higher percentage among patients whose
neurosurgeons had performed fewer than 500 microsurgical
transsphenoidal operations ( Table 6).

TABLE 6
Percentage of complications resulting from transsphenoidal pituitary surgery

<table>
<thead>
<tr>
<th>Type of Complication</th>
<th>No. of Ops</th>
<th>Present Study</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;200</td>
<td>200–500</td>
</tr>
<tr>
<td>septal perforation</td>
<td>7.6</td>
<td>4.6</td>
</tr>
<tr>
<td>epistaxis</td>
<td>4.3</td>
<td>1.7</td>
</tr>
<tr>
<td>sinusitis</td>
<td>9.6</td>
<td>6.0</td>
</tr>
<tr>
<td>CA injury</td>
<td>1.4</td>
<td>0.6</td>
</tr>
<tr>
<td>CNS injury</td>
<td>1.6</td>
<td>0.9</td>
</tr>
<tr>
<td>hemorrhage/swelling</td>
<td></td>
<td></td>
</tr>
<tr>
<td>of residual tumor</td>
<td>2.8</td>
<td>4.0</td>
</tr>
<tr>
<td>loss of vision</td>
<td>2.4</td>
<td>0.8</td>
</tr>
<tr>
<td>ophthalmoplegia</td>
<td>1.9</td>
<td>0.8</td>
</tr>
<tr>
<td>CSF leakage</td>
<td>4.2</td>
<td>2.8</td>
</tr>
<tr>
<td>meningitis</td>
<td>1.9</td>
<td>0.8</td>
</tr>
<tr>
<td>anterior pituitary</td>
<td></td>
<td></td>
</tr>
<tr>
<td>insufficiency</td>
<td>20.6</td>
<td>14.9</td>
</tr>
<tr>
<td>diabetes insipidus</td>
<td>19.0</td>
<td>7.6</td>
</tr>
<tr>
<td>death</td>
<td>1.2</td>
<td>0.6</td>
</tr>
</tbody>
</table>

* Modified from Ciric, et al.

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Acknowledgment

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