Review

Microscopic versus endoscopic pituitary surgery


A B S T R A C T

Introduction and objective: The endoscopic techniques used in pituitary surgery have evolved greatly in recent years. Our objective in this study was to conduct a review of the systematic reviews published in the English language literature, to examine their consistency and conclusions reached following studies comparing microsurgery and endoscopic surgery in hypophyseal surgery.

Materials and methods: We carried out a bibliographic search on MEDLINE and EMBASE electronic databases, selecting those systematic reviews and meta-analyses published from the year 2000 until January 2013, focusing on comparisons between microsurgical and endoscopic techniques.

Results: We concluded with type A consistency that hospital stay was shorter and diabetes insipidus and rhinological complications were less frequent in the endoscopy group. We concluded with type B consistency that lower rates of patient blood loss, shorter operative times, higher rate of gross total resection, lesser association to visual impairment and lower rate of hypopituitarism were observed in the endoscopy group. Vascular complications and cerebrospinal fluid fistulas were reduced with microsurgery. It is crucial to perform a combined analysis of all the systematic reviews treating a specific topic, observing and analysing the trends and how these are affected by new contributions.

Conclusion: Randomized multicenter studies are necessary to resolve the controversy over endoscopic and microsurgical approaches in hypophyseal pathology.

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Cirugía hipofisaria microscópica versus endoscópica

Resumen

Introducción y objetivo: Las técnicas endoscópicas aplicadas a la cirugía hipofisaria han experimentado un importante desarrollo en los últimos años. Nuestro objetivo es realizar un examen de las diferentes revisiones sistemáticas publicadas en la literatura inglesa, para
Cirugía endoscópica
determinar la consistencia y las conclusiones alcanzadas tras la comparativa entre abordajes endoscópicos y microscópicos en la cirugía hipofisaria.

Material y métodos: Se ha realizado una revisión de la literatura inglesa utilizando las bases de datos MEDLINE y EMBASE, seleccionando las revisiones sistemáticas y metaanálisis publicados desde el año 2000 al 2013, focalizándonos en la comparativa entre los abordajes endoscópicos y microscópicos para el tratamiento de patología hipofisaria.

Resultados: Concluimos con consistencia tipo A que la estancia hospitalaria fue más corta, así como la diabetes insípida y las complicaciones rinitológicas fueron menos frecuentes en el grupo endoscópico. Encontramos consistencia tipo B a favor de que la pérdida hemática es menor, el tiempo quirúrgico es más corto, la tasa de resección completa es mayor, el deterioro visual es menos frecuente y la tasa de hipopituitarismo es menor en el grupo endoscópico. Las complicaciones vasculares y la fistula de LCR fueron menos frecuentes en el grupo microscópico con consistencia tipo B. Resulta fundamental realizar un análisis combinado de todas las revisiones sistemáticas que tratan un tema específico, observando y analizando las tendencias y cómo estas se pueden ver afectadas por las nuevas contribuciones.

Conclusiones: Estudios aleatorizados multicéntricos son necesarios para resolver la controversia entre el tratamiento endoscópico y microscópico de la patología hipofisaria.

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The endoscopic techniques used in skull base and pituitary surgery have evolved greatly in recent years, as well as in our academic circle,\(^1\)\(^{-}\)\(^3\) propelled by technology advances. Evidence-based medicine demands a firm foundation of practical experience to provide a sufficiently broad sample size to detect differences between new and classical techniques. Thus it is imperative to conduct studies with high evidentiary value as well as meta-analysis and systematic reviews to confirm the soundness of new endoscopic advances. Our objective in this study was to conduct a review of published English language literature systematic reviews (SRs), to examine consistency of their results and conclusions reached on studies comparing microsurgery and endoscopic surgery in hypophyseal surgery.

Materials and methods
We conducted a SR of the English language literature from the year 2000 until January 2013. We carried out a bibliographic search on MEDLINE and EMBASE electronic databases selecting those systematic reviews and meta-analyses published over a thirteen-year period on hypophyseal surgery, focusing on microsurgical and endoscopic technique comparisons. Search terms used were: systematic review, meta-analyses, endoscopy, endonasal, microscopy, pituitary adenoma and pituitary surgery. Additionally, extensive hand searching of the references for all relevant studies was performed. From these search results two reviewers selected studies that dealt with treatment of hypophyseal adenomas. PRISMA checklists were used and fulfilled. The inclusion criteria were systematic reviews and meta-analyses focusing on microsurgical and endoscopic technique comparisons for pituitary adenomas, with at least one variable considered with respect to the outcome or complication assessment (length of hospital stay, diabetes insipidus, intraoperative blood loss, operative time, gross total remove, anterior hypopituitarism, visual impairment, CSF leak, vascular, rinitological or infectious complications, death). Exclusion criteria were: review with no available direct comparison between the endoscopic and microscopic procedures and review focused on only one type of adenoma (giant, non functional or functional adenomas). Included studies were assessed indicating the quality of methodology used in the study. Levels of evidence were defined using commonly accepted standards in the literature, as follows: randomized controlled trials (level 1), prospective or retrospective cohort studies and poor quality randomized controlled trials (level 2), case control studies (level 3), case series or observational studies (level 4), and case reports and expert opinion (level 5) (Table 1). After analyzing the studies, we identified several levels of consistency among the reviews defined in Table 2, depending on their statistical significance and the homogeneity of their results.

Results
Six comparative reviews met these inclusion criteria, but in the oldest, published in 2009 by Tabaei et al.,\(^4\) only 3 studies used control groups, which were very heterogenous, making it impossible to perform comparative analysis between the two techniques, and in the Komotor et al.\(^5\) review, published in 2012, only the giant pituitary adenomas were had in account, thus both these two reviews were excluded (Fig. 1). Finally, only four reviews\(^6\)\(^{-}\)\(^9\) met the inclusion criteria, directly comparing microsurgery and endoscopic surgery. Below is our detailed discussion along the following dimensions:

General data and time perspective
In 2010 Rotenberg et al.\(^6\) published the first systematic review of English language publications up to June 2009, selecting studies that directly compared research on microsurgery versus endoscopy and excluding low-evidence studies. 11 studies met the inclusion and exclusion criteria.\(^10\)\(^{-}\)\(^20\) The endoscopic approach decreased operating time, lumbar drains,
Table 1 – Quality and evidence of studies included.

<table>
<thead>
<tr>
<th>Quality and evidence of studies included</th>
<th>Inclusion</th>
<th>Exclusion criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tabaei 2009</td>
<td>NO</td>
<td>No direct comparison between endoscopic/microscopic</td>
</tr>
<tr>
<td>Rotenberg 2010</td>
<td>YES</td>
<td></td>
</tr>
<tr>
<td>Goudakos 2011</td>
<td>YES</td>
<td></td>
</tr>
<tr>
<td>Komotar 2012</td>
<td>YES</td>
<td></td>
</tr>
<tr>
<td>Ammirati 2012</td>
<td>YES</td>
<td></td>
</tr>
</tbody>
</table>

Table 2 – Levels of consistency.

<table>
<thead>
<tr>
<th>Consistency type</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Uniform results across systematic reviews, with one or more of them showing statistically significant differences</td>
</tr>
<tr>
<td>B</td>
<td>Heterogenous results across reviews, with some differences showing statistical significance. Uniform results within most reviews while not quite reaching either statistical significant differences</td>
</tr>
<tr>
<td>C</td>
<td>Heterogenous results across systematic reviews, with isolated uniformity in quantitative reviews</td>
</tr>
<tr>
<td>D</td>
<td>Globally heterogeneous results across systematic reviews</td>
</tr>
</tbody>
</table>

Fig. 1 – Flow diagram demonstrating the systematic analysis process (Preferred Reporting Items for Systematic Reviews and Meta-Analyses Guidelines flow diagram).

immediate postoperative diabetes insipidus, some rhinologic complications, length of hospital stay, and patient pain and discomfort. Other outcome measures were comparable between the two approaches. One year later, Goudakos et al.\textsuperscript{7} conducted SR and meta-analysis of the English language studies comparing transphenoidal sublabial and transseptal microsurgery against endoscopic surgery, for those studies where at least 20 patients received treatment in the same medical facility and had complete outcome records. 11 studies met these criteria\textsuperscript{11,12,15-23} including 806 patients (endoscopic group = 369, microscopic group = 437). The majority of included studies were retrospective case series. Two studies are randomized trials, with only one of them using a true randomization method. Remission rates for hypersecreting adenomas were around 66% for endoscopy versus 60% for microsurgery, without statistically significant differences. For total resection the rate was higher for endoscopy, 71% versus 69%, and also did not reach statistical significance. As for complications, the rate for cephalorachidian fistulas was 19.5% for endoscopy versus 14.7% for microsurgery, without reaching statistical significance. Post-operative transient and permanent diabetes insipidus was less frequent in those having endoscopic surgery compared with the microscopic group with statistically significant differences (15 versus 28% and 2 versus 10%). The authors categorized the complications as either surgery-related (epistaxis, anosmia, nasal anesthesia, lip anesthesia, septal perforation deviated septum and synchieae) or resulting from poor surgical technique (meningitis, encephalitis, loss of visual acuity and pneumocephalus). Complications were fewer for endoscopy with statistically significant differences. Average hospital stay was likewise significantly shorter for the endoscopy treatment group.

In 2011 Strychowsky et al.\textsuperscript{8} also published an SR up to October 2009, to establish whether endoscopic intervention can improve surgical results for hypophysial adenomas or reduce complications. They selected studies comparing both techniques and had data for at least one of the major variables, gross tumor resection (GTR), recurrence, visual field improvement, hormone resolution, mean blood loss, mean operative time, mean hospital length of stay, cerebrospinal fluid (CSF) leak, hormone deterioration, vision deterioration, nasal complications, meningitis, and death. They included 10 studies,\textsuperscript{11,12,15,18,20-23} only one of them prospective, encompassing 687 patients. Endoscopy was associated with lower intraoperative blood loss, lower rate of rinhological complications, shorter hospital stay and shorter operative time. Endoscopy was also associated with improved total resection and diabetes insipidus rates, while microsurgery tended to reduce fistulas.

Toward the end of 2012 Ammirati et al.\textsuperscript{9} published a meta-analysis and review of English language publications. They included studies with more than 10 patients treated with either microsurgery or endoscopy. This review analyzed a total of 5643 patients, of which 2125 were operated using the endoscope and 3518 using the microscope.\textsuperscript{11,15,17,20,21,23-54} The results for the microsurgery and endoscopy cohorts were 0.23% versus 0.49%, csf leak 6.34 versus 7%, meningitis 2.08 versus 1.11%, vascular complication 0.5 versus 1.58%, visual loss 0.60 versus 0.72%, diabetes insipidus temporary 10.23
versus 9.10% and permanent 4.25 versus 2.31%, hypopituitarism 1164 versus 8.51%, nerve injury 0.53 versus 0.28% and complete resection 64.44 versus 68.77% respectively. Only the differences related to vascular complications reached statistical significance. The authors concluded that endoscopy is associated with higher rates of adverse vascular events.

**Systematic review general methodology**

Of the four SRs analyzed, two were qualitative (Rotenberg et al. and Strychowsky et al.) and two quantitative (Goudakos et al. and Ammirati et al.), thus only the latter can show statistically significant differences. On the other hand, not all variables were taken into account in all the reviews.

**Study inclusion**

Three reviews included only direct comparisons between microsurgery and endoscopy, while one review also includes individual endoscopy or microsurgery series. Inclusion criteria were also heterogeneous in terms of study quality, the quality and evidence of each study included in the systematic review are described in Table 1; only two reviews considered minimal criteria on outcome data required for studies to be included. Endoscopy-assisted procedures are likewise treated heterogeneously in the published SRs; some of them included these procedures in one of their groupings and some did not.

**Analysis of results**

**Blood loss**

Strychowsky et al. concluded that there was less blood loss in the endoscopy treatment group, while Goudakos et al. did not find statistical significance for this variable but did find the same tendency to favor endoscopy (consistency B).

**Operative time**

Endoscopy also resulted in shorter operative duration, and again the quantitative review of Goudakos et al. did not show statistically significant differences but did show a trend in favor of endoscopy (consistency B).

**Hospital stay**

Length of hospital stay was lower with endoscopy in the two qualitative reviews that looked at this variable, and in this case the review by Goudakos et al. did find statistically significant differences in favor of endoscopy (consistency A).

**Resection**

Total resection rates were similar in the SR by Rotenberg, while reviews by Strychowsky, Goudakos and Ammirati found higher total resection rates in the endoscopy group, though the differences were not statistically significant (consistency B).

**Hypopituitarism**

Anterior hypopituitarism was similar in the qualitative reviews of Rotenberg and Strychowsky, while in quantitative studies Goudakos and Ammirati found lower rates in the endoscopy group, though not statistically significant (consistency B).

**Diabetes insipidus**

All the systematic reviews found lower rates of postoperative diabetes insipidus after endoscopic surgery, highlighting the statistically significant differences in the review of Goudakos (consistency A).

**Cephalorachidian fluid fistula**

Rotenberg found that endoscopic procedures reduced the placement of lumbar drains in comparison to microsurgical procedures. Strychowsky, Goudakos and Ammirati found higher frequency of fistulas in the endoscopy group, but none of the reviews found statistical significance (consistency B).

**Rhinologic complications**

The two qualitative reviews found lower frequencies with endoscopic surgery; Goudakos found statistical significance while Ammirati did not analyze this variable (consistency A).

**Visual outcome**

All reviews analyzed visual deterioration. Rotenberg and Strychowsky found similar results for endoscopy and microsurgery, while Goudakos and Ammirati found lower rates in endoscopy, without statistical significance (consistency B).

**Intradural meningitis/encephalitis**

Infectious events were similar in the reviews of Rotenberg, Strychowsky and Goudakos. In Ammirati’s meta-analysis the rate of meningitis was lower after endoscopic surgery, without statistical significance (consistency C).

**Vascular complications**

Their classification for the various series was heterogeneous. Ammirati included internal carotid arterial injuries, damages to less important vessels like the sphenopalatine artery, intracranial or sellar hemorrhages, ischemic infarcts, and cavernous sinus bleeding, detecting statistically significant lower rates of vascular adverse events for microsurgery with statistical significance. Goudakos did not strictly consider vascular complications, but included the analyses that were not related to surgery complications, hemiplegia and stroke, more frequent in microscopic cohort but without statistical significance (consistency B).
Death rate

None of the SRs found statistically significant differences between microsurgery and endoscopy, while there was disparity of results in the quantitative reviews. Goudakos found higher death rates for microsurgery while Ammirati did so for endoscopy (consistency D).

These categorized results are summarized in Tables 3 and 4.

Discussion

The first three SRs to be published by Rothenberg, Goudakos, Strychowsky et al. drew similar conclusions, or at least directionally similar, finding shorter hospital stays and operative durations for endoscopy, with higher patient tolerance and lower rates of diabetes insipidus and nasal complications. Total resection and hypopituitarism tended to be lower but without statistical significance. In contrast, in the last meta-analysis Ammirati et al. found no differences favoring endoscopy in any of the variables examined, existing higher rate of vascular complications in the endoscopic cohort with statistical significance. Given the different conclusions by the various authors, we believe it is more practical to evaluate all the reviews together, with a predetermined methodology weighing the various conclusions, thus we defined a consistency classification mechanism in ‘Materials and Methods’.

The first series of purely endoscopic studies for treatment of hypophyseal adenomas was published by Jho and Cerrado in 1997. On the other hand, microsurgery has received broad coverage since the 1950s when it was introduced together with fluoroscopy. Only in the last 3 years systematic reviews and meta-analyses have been published comparing the two techniques. A major reason for this is that endoscopy is still rather new, also explaining the shorter number of patients of endoscopic studies compared with microsurgery, as reflected in Ammirati’s meta-analysis, in which four microsurgery studies described sets of 1140, 638, 592 and 208 patients; meanwhile, eight microsurgery studies described the treatment of only functional tumors, and six of the reviewed studies included more than 50 acromegalgies or Cushing’s syndrome cases, implying that the surgeons in question treated a significant number of adenomas. On the other hand, only one endoscopic study of the 24 selected had more than 200 patients.

After analyzing the SRs, as well as the evolutive factor before mentioned, the heterogeneity about the inclusion criteria, number of patients treated, existence of complete outcome and the variability in the definition of endoscopic assisted procedure attracts attention. Ammirati et al. stated in their analysis that they included in the microsurgery group those studies where endoscopy was used to guide the surgical approach but tumor resection was done with microsurgery. Ammirati also included as pure microsurgery the study by Mortini et al. where the authors state that after resection of the adenoma, the cavity was scanned by endoscopy. We should point out that the term “endoscopy assisted” covers all procedures where an endoscope is used in some aspect of microsurgery, either for surgical approach, preparation of the surgical site or guidance during resection. Inclusion of this study in Ammirati’s meta-analysis, contributing 32.4% of the total microsurgery cohort, is rather unorthodox. The use of intraoperative endoscopy after microscopic resection provides the advantages of endoscopic procedures, such as better visualization of structures and of lateral and suprasellar limits, as well as differentiation between normal and diseased tissue. Inclusion of these patients introduces significant bias, strongly favoring microsurgery by giving it the advantages of endoscopy, and complicating a comparison between the two methods.

The primary feature of our review is the evaluation of the combined results (Table 3). We concluded with consistency A that hospital stay was shorter, diabetes insipidus and rhinological complications were lower in the endoscopy group and found with consistency B lower rates of patient blood loss, shorter operative time, higher rate of gross total remove, lesser association to visual impairment and lower rate of hypopituitarism with endoscopy but lower cephalorachidian fluid fistulas and vascular complications with microsurgery. As for intradural infectious processes and death, there was scant consistency in favor of either procedure. Ours is the first published study that uses published systematic reviews to consider the strength of various conclusions in the area of hypophyseal surgery.

Ammirati’s analysis of vascular complications merits special attention. The variety of complications that were grouped together as vascular complications was highly heterogeneous, encompassing carotid lesions, lesions in less important vessels like the sphenopalatine artery, intracranial or sellar hemorrhages, ischemic infarcts, and cavernous sinus bleeding. While all of these complications are of a vascular nature, their characteristics and the resulting morbidity/mortality can be quite different. The limitations of microsurgery for treatment of significant invasions into the cavernous sinus are well known. Thus, when approaching an invasive cavernous sinus adenoma endoscopically for treatment, as in the study by Zhang et al., consideration of vascular complications from

<table>
<thead>
<tr>
<th>Consistency</th>
<th>Endoscopic favorable result</th>
<th>Microscopic favorable result</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Length of hospital stay, diabetes insipidus and rhinological complications</td>
<td>CSF leak, vascular complications</td>
</tr>
<tr>
<td>B</td>
<td>Blood loss, operative time, gross total remove, anterior hypopituitarism, visual impairment</td>
<td>Intradural infectious procedure Death</td>
</tr>
<tr>
<td>C</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D</td>
<td></td>
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<td>-------------------------</td>
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</tr>
<tr>
<td><strong>Number of studies</strong></td>
<td>11 studies, 547 patients (234 endoscopic, 313 microscopic)</td>
<td>11 studies, 806 patients (369 endoscopic, 437 microscopic)</td>
</tr>
<tr>
<td><strong>Blood loss</strong></td>
<td>Not specified</td>
<td>Not specified</td>
</tr>
<tr>
<td><strong>Operation time</strong></td>
<td>Two studies showed shorter times for endoscopy and other two found no significant differences. No difference in set-up time</td>
<td>Meta-analysis not significantly different</td>
</tr>
<tr>
<td><strong>Hospital stay</strong></td>
<td>Endoscopic 3.2–3.7 days Microscopic 5.3–8.3 Length of stay was shorter for endoscopy in all studies</td>
<td>Endoscopic 3.7–4.4 days Microscopic 5.4–5.7 days (p &lt; 0.00001)</td>
</tr>
<tr>
<td><strong>Tumor resection</strong></td>
<td>Efficacy of tumor debulking was comparable between both groups</td>
<td>Trend for higher resection in endoscopic group</td>
</tr>
<tr>
<td><strong>Hypopituitarism</strong></td>
<td>Not significantly different</td>
<td>Lower rates of hypopituitarism in endoscopic group were not significant</td>
</tr>
<tr>
<td><strong>Diabetes insipidus</strong></td>
<td>Immediate DI: significantly lower in endoscopic cases Long-lasting: No significant differences</td>
<td>Endoscopic: 15% Microscopic: 28% (p = 0.003)</td>
</tr>
<tr>
<td><strong>CSF leak</strong></td>
<td>In six of seven studies describing general rates of postoperative CSF, no significant difference was found</td>
<td>Not significantly different</td>
</tr>
<tr>
<td><strong>Rhinological</strong></td>
<td>Significantly greater in microscopic approach, although olfactory disturbances and crusting remain insufficiently studied to make a formal comparison</td>
<td>Endoscopic 1.2% Microscopic 13% (p &lt; 0.05)</td>
</tr>
<tr>
<td><strong>Visual outcome</strong></td>
<td>Not significantly different</td>
<td>Loss of visual acuity endoscopic 0.3%, microscopic 0.78%, differences not significant</td>
</tr>
<tr>
<td><strong>Infection</strong></td>
<td>Not significantly different</td>
<td>Not significantly different</td>
</tr>
<tr>
<td><strong>Vascular complications</strong></td>
<td>Not specified</td>
<td>Incidence of hemiplegia and stroke were higher in microscopic group but differences were not significant</td>
</tr>
<tr>
<td><strong>Death rate</strong></td>
<td>Not specified</td>
<td>Endoscopic: no death Microscopic: 0.52%</td>
</tr>
</tbody>
</table>
cavernous sinus bleeding is not comparable to microsurgical approach cases where there was no initial intention to treat invasive cavernous sinus tumors. The surgeon’s experience level in the included studies is a variable seldom evaluated across reviews, though it has been examined sometimes within reviews as a learning-curve effect referred to by many authors. In 1997 Ciric et al. categorized microsurgery results and complications based on the surgeon’s experience: less than 200 surgeries, 200–500 surgeries, and over 500 surgeries. They found a death rate of 0.2%, cSf leak 1.5%, meningitis 0.5%, vascular complication (carotid artery injury + hemorrhage residual tumor) 1.2%, visual loss 0.5%, diabetes insipidus 7.6%, hypopituitarism 7.2% in the most experienced cases. Taking this experience level into account for the microsurgery findings in Ammirati’s meta-analysis, for variables as important as vascular complications, death, diabetes insipidus and hypopituitarism, the microsurgery group turns out to be a select group of patients with better results than those of the most experienced microscopic surgeons in Ciric’s study. Therefore the meta-analysis has a hyperselected cohort for microsurgery, probably due to a number of factors. Ammirati’s meta-analysis results could be due to many reasons, such as those suggested above, including: a series of patients with a high incidence of microadenomas (based on available data of Ammirati study, we can only be certain that 57.6% (2027/3518) of the microscopic patients were microadenomas, whereas 77% (1453/1887) of the cases were macroadenomas in the endoscopic cohort); inclusion of endoscopy-assisted cases in the microsurgery group; the long tradition and evolution of microsurgery since the 1950s versus the recent history of purely endoscopic techniques (first series reported in 1997).

It is possible that a truly randomized multicenter study may never be done for hypophyseal pathology, or if it is done, it may not include variables like surgical experience, which are hard to evaluate. Experienced microsurgeons and endoscopy surgeons tend to treat hypophyseal pathology in an optimal way, so that a change in standard of treatment would not make sense. On the other hand, even taking into account their short history, endoscopic approaches have tended to produce significant improvements in almost all variables related to hypophyseal pathology. This fact goes hand in hand with the great advances in endoscopic cranial base surgery, which now makes it possible to treat highly complex pathologies in difficult to reach locations with better results than ever, such as the clivus or the anterior cranio-cervical junction. For all this, we think that endoscopic surgery education and training is a good bet for the near future.

**Limitations**

The heterogenous treatment of almost all of the variables analyzed by SRs clearly shows the limitations of this type of review. As for the meta-analysis methodology, depending on the heterogeneity between studies, fixed effect models or randomized models were applied. Randomized models provide more conservative estimates than fixed effect models, and therefore are more apt to miss existing differences. These methods were used to compare rates of diabetes insipidus, hypopituitaritism, and complete resection. All trends toward favoring the endoscopy group in the most SR, but without statistical significance. Repeat trend analysis in the various SRs should be examined, not only the statistical significance. In our consistency model we tried to determine the weight of each result in the included reviews, and while this approach has not been validated we think it can be useful and intuitive. The difficulty in measuring and comparing important variables such as surgical experience is another limitation of this study.

**Conclusion**

The presence or absence of evidence in a systematic review should be examined conservatively. It is fundamental to perform a combined analysis of all the reviews that treat a specific theme, observing and analyzing the trends and how these are affected by new contributing studies. We think it is imperative to conduct studies to evaluate the various conclusions, especially when they are contradictory. In the field of hypophyseal surgery and in the absence of studies with strong evidence, this type of review can assess the strength of results from prior reviews. Randomized multicenter studies are necessary to resolve the controversy over endoscopic and microsurgical approaches in hypophyseal pathology.

**Conflicts of interest**

The author has no conflicts of interest to declare.

**References**


