Neurosurgical Subspecialties **2025** vol. 1(1) | 39–43
DOI: 10.14218/NSSS.2024.00008

Mini Review

Advances in Neuroendoscopic Treatment of Pituitary Tumors

Xing Huang and Xiaobing Jiang*

Department of Neurosurgery, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei, China

Received: November 26, 2024 | **Revised:** March 10, 2025 | **Accepted:** March 18, 2025 | **Published online:** March 25, 2025

Abstract

Pituitary tumors are common intracranial neoplasms that can cause significant morbidity due to hormonal dysregulation and compression of surrounding structures. Despite advancements in surgical techniques, challenges persist in treating large, invasive, or recurrent tumors, where complete resection is often difficult. The molecular and genetic mechanisms underlying pituitary tumorigenesis are not yet fully understood, limiting the development of targeted therapies. This review provides a comprehensive overview of recent advancements in neuroendoscopic treatment of pituitary tumors, with a focus on pathogenesis, technological innovations, clinical outcomes, and future directions. We highlight the potential of neuroendoscopic surgery to improve patient outcomes while addressing persistent challenges, such as the steep learning curve and limitations in instrument maneuverability. Future research should prioritize enhancing instrument design, developing 3D and augmented reality visualization systems, and improving training programs to further advance neuroendoscopic techniques.

Introduction

Pituitary tumors are among the most common intracranial neoplasms, accounting for approximately 10–15% of all brain tumors.[1] Although typically benign, these tumors can cause significant morbidity due to hormonal dysregulation and compression of surrounding structures, such as the optic chiasm and cranial nerves. The management of pituitary tumors has evolved considerably over the past few decades, shifting toward minimally invasive surgical techniques that reduce patient morbidity while achieving optimal tumor resection.

Historically, pituitary tumor treatment relied heavily on open craniotomy and microscopic transsphenoidal surgery. While effective, these approaches were associated with significant surgical trauma, prolonged recovery times, and higher complication rates.[2] The advent of neuroendoscopic technology has revolutionized the field, offering a less invasive alternative with enhanced visualization and precision. Neuroendoscopic transsphenoidal surgery has emerged as the gold standard for many pituitary tumors, enabling surgeons to access tumors via the nasal cavity without requiring a cranial opening.

Despite these advancements, challenges remain in treating large, invasive, or recurrent tumors, where complete resection remains difficult.[3] Additionally, the molecular and genetic mechanisms underlying pituitary tumorigenesis are not yet fully understood,[4] limiting the development of targeted therapies. This review aimed to provide a comprehensive overview of recent advancements in the neuroendoscopic treatment of pituitary tumors, focusing on pathogenesis, technological innovations, clinical outcomes, and future directions. By synthesizing current evidence and offering our perspectives, we aimed to highlight the potential of neuroendoscopic surgery to improve patient outcomes and guide future research in this field.

We conducted an extensive search across multiple authoritative databases, including PubMed, Medline, Embase, Web of Science, and Cochrane Library, using keywords such as "neuroendoscopic surgery," "pituitary tumors," "transsphenoidal surgery," "biochemical remission," "suprasellar approach," "cavernous sinus approach," and "pituitary adenoma subtypes." The search was limited to English-language articles published between 2000 and 2023. Case reports, editorials, non-English publications, and studies with insufficient data or unclear methodologies were excluded.

Pathogenesis of pituitary tumors

Pituitary tumors, arising from the pituitary gland at the base of the brain, constitute a significant proportion of intracranial neoplasms. Although often benign, these tumors can profoundly impact hormone secretion and overall health. Their development can be conceptually divided into two stages: initiation and progression. During the initiation stage, genetic and epigenetic alterations in pituitary cells activate oncogenes and inactivate tumor suppressor genes, setting the stage for cellular transformation.[5] In the progression stage, environmental stimuli, endocrine dysregulation, and aberrant signal-

Keywords: Neuroendoscopic technology; Pituitary tumors; Pathogenesis; Technical improvement; Clinical outcomes; Technical limitations.

***Correspondence to:** Xiaobing Jiang, Department of Neurosurgery, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei 430022, China. ORCID: https://orcid.org/0000-0002-1121-0770. Tel: +86-85350772, E-mail: 2004xh0835@hust.edu.cn

How to cite this article: Huang X, Jiang X. Advances in Neuroendoscopic Treatment of Pituitary Tumors. *Neurosurg Subspec* 2025;1(1):39–43. doi: 10.14218/NSSS.2024.00008.

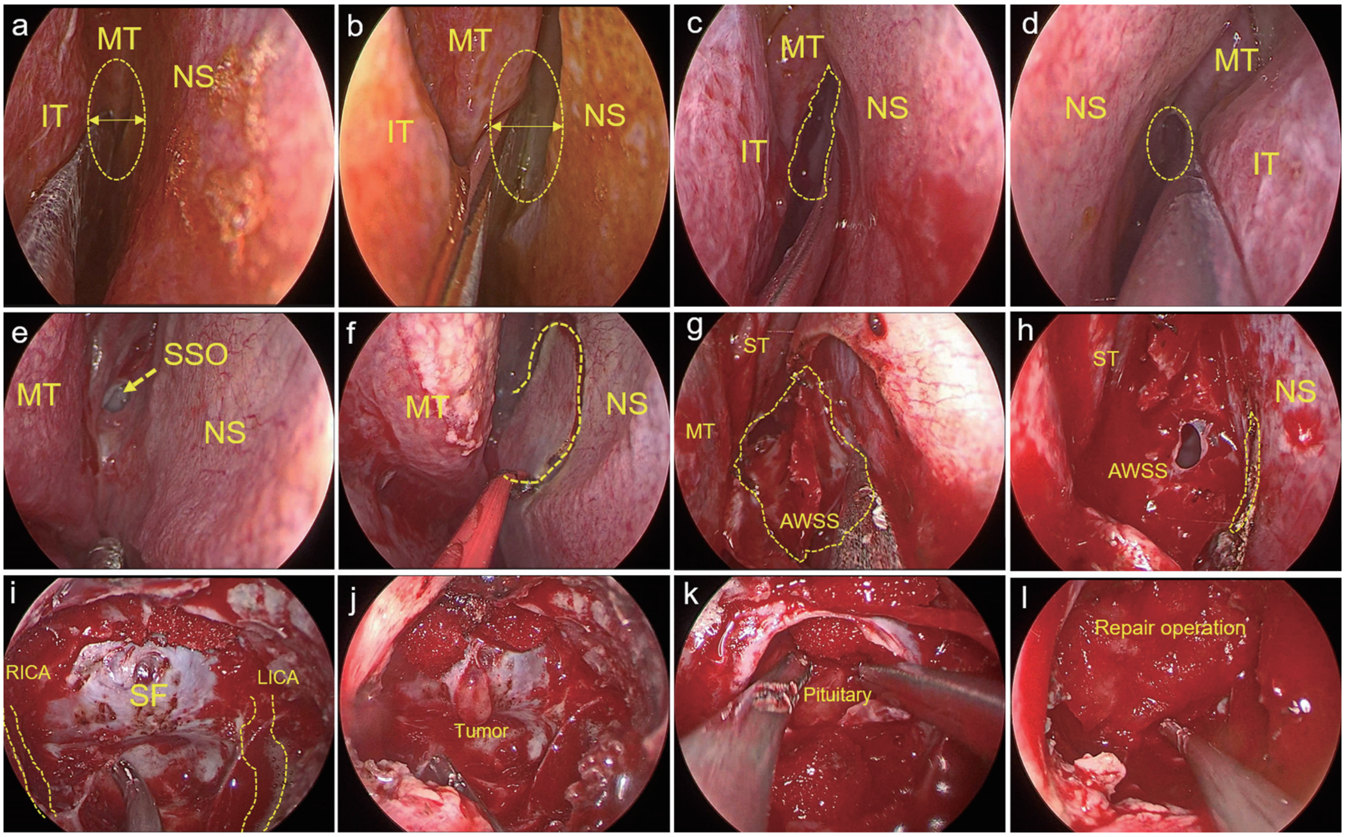

Fig. 1. Classic transnasal resection of pituitary tumors in the sellar region. (a–d) Initial tumor exposure through the nasal cavity, with the inferior turbinate (IT) and nasal septum (NS) visible. (e–h) Visualization of the sphenoid sinus opening (SSO) and anterior wall of the sphenoid sinus (AWSS). (i–l) Complete tumor resection with clear visualization of the sphenoid sinus and surrounding structures. LICA, left internal carotid artery; MT, middle turbinate; RICA, right internal carotid artery; SF, sellar floor; ST, superior turbinate.

ing cascades promote the proliferation and invasion of transformed cells, ultimately leading to clinically apparent pituitary tumors.[6]

The onset of pituitary tumors is often preceded by genetic alterations.[5] Mutations in oncogenes and the inactivation of tumor suppressor genes have been implicated in their initiation and progression. For instance, activation of the guanine nucleotide-binding protein alpha subunit (gsp) oncogene is prevalent in growth hormone-secreting pituitary tumors.[7] Additionally, mutations in the multiple endocrine neoplasia type 1 gene,[8] a tumor suppressor, have been linked to familial pituitary tumor syndromes. These genetic alterations disrupt the delicate balance of cell growth and proliferation, favoring tumor development.

The progression of pituitary tumors involves intricate molecular pathways. Aberrant signaling cascades, mediated by growth factors and their receptors, play a pivotal role. Growth hormone-releasing hormone and its receptor promote the growth of growth hormone tumors.[9] Similarly, overexpression of platelet-derived growth factor, transforming growth factor-alpha, and transforming growth factor-beta has been observed in various pituitary tumors,[10] driving cellular proliferation and differentiation. Furthermore, dysregulation of intracellular signaling pathways,[11] including MAPK/ERK and PI3K/Akt/mTOR, contributes to the unchecked growth of pituitary tumor cells. Given their role in pituitary tumor progression, targeted therapies inhibiting these pathways hold promise, particularly for tumors resistant to conventional treatments.

Pituitary tumors can disrupt normal endocrine function by either hypersecreting hormones or compressing adjacent structures,[12] leading to hormone deficiency. Functioning pituitary tumors, such as prolactinomas and growth hormone tumors, overproduce hormones like prolactin and growth hormone, respectively, causing characteristic clinical symptoms. Conversely, non-functioning pituitary tumors, while not secreting excess hormones, can grow large enough to compress the normal pituitary gland, impairing its ability to secrete essential hormones and resulting in endocrine deficiencies.

Environmental factors also play a role in pituitary tumor development.[13] Exposure to radiation, toxic chemicals, and certain medications has been linked to an increased risk of pituitary tumors. Additionally, lifestyle factors such as obesity, physical inactivity, and stress may contribute to endocrine disturbances that indirectly contribute to pituitary tumor development.

Neuroendoscopic technology

Neuroendoscopic technology has revolutionized neurosurgery,[14] offering a minimally invasive alternative to traditional open procedures for various intracranial pathologies. This innovative technique leverages advanced optics and precision instrumentation to navigate intricate intracranial spaces with unparalleled visualization and reduced surgical trauma. Neuroendoscopic surgery offers a minimally invasive approach to pituitary tumor resection through the natural nasal cavity (Fig. 1).

The evolution of pituitary tumor surgery has progressed remarkably, starting with single and double-nostril approaches, which provided minimally invasive access but had limitations in handling complex or invasive tumors. This was followed by the development of the expanded suprasellar approach for tumors extending above the sella turcica. More recently, the lateral cavernous sinus approach has enabled the resection of tumors invading the cavernous sinus, a region previously considered challenging to access endoscopically.[3,15] Neuroendoscopic transsphenoidal surgery has demonstrated significant improvements in tumor resection rates and biochemical remission rates across various pituitary tumor subtypes. Studies have shown that neuroendoscopic techniques achieve higher gross total resection (GTR) rates compared to traditional microscopic approaches, with GTR rates reaching 87.9% in neuroendoscopic groups versus 66.0% in microscopic groups, particularly for non-functioning pituitary adenomas.[16] This is attributed to the enhanced visualization and maneuverability of the endoscope, which facilitates more complete tumor removal, even in large or invasive cases. In prolactinomas, neuroendoscopic surgery has achieved biochemical remission rates of 70–90% for microprolactinomas and 30–50% for macroprolactinomas, providing an effective alternative for patients resistant to medical therapy. For growth hormone-secreting tumors (acromegaly), remission rates have improved to 60–80%, particularly for macroadenomas, due to better access to lateral extensions and improved visualization of tumor margins. For Cushing's disease (Adrenocorticotropic hormone secreting tumors), neuroendoscopic surgery has achieved remission rates of 80–95% for microadenomas and 60–70% for macroadenomas, significantly reducing recurrence rates and preserving pituitary function. For non-functioning pituitary adenomas, neuroendoscopic surgery has resulted in GTR rates of 70–90%, with lower recurrence rates and better preservation of pituitary function compared to traditional approaches. These outcomes highlight the transformative impact of neuroendoscopic surgery on the management of pituitary tumors, offering patients safer and more effective treatment options.

This technique eliminates the need for cranial opening, significantly reducing surgical trauma, postoperative pain, and hospital stay.[17] Additionally, patients recover faster and experience improved quality of life. The flexible design of neuroendoscopes enables multi-directional and multi-angle adjustments, enabling access to challenging areas within the pituitary gland. This increased maneuverability enhances surgical safety and effectiveness.

Advancements in neuroendoscopic technology

High-resolution imaging and visualization

One of the key advancements in neuroendoscopic technology is the improvement in imaging and visualization capabilities.[18] High-definition cameras, three-dimensional endoscopy, and advanced optical systems have significantly enhanced surgeons' ability to visualize and navigate within the intracranial space. These improvements allow for more precise dissection, resection, and reconstruction, ultimately reducing surgical trauma and improving patient outcomes.

Miniaturization and flexibility

The miniaturization and increased flexibility of neuroendoscopes have been crucial in the evolution of this technology.[2] The development of thin, flexible endoscopes has enabled surgeons to access previously unreachable areas, such as the skull base and deep brain regions. This enhanced accessibility has expanded the indications for neuroendoscopic surgery, making it a viable option for increasingly complex procedures.

Computer-assisted navigation and robotics

The integration of computer-assisted navigation systems and robotics into neuroendoscopy represents a significant leap forward. These technologies enhance surgical accuracy and precision, reducing human error and improving patient outcomes.[19] Real-time imaging, spatial tracking, and robotic manipulation capabilities are transforming the way neuroendoscopic procedures are performed, allowing for safer and more effective surgeries.

The chopsticks technique

Developed by French neurosurgeon Sebastien Froelich, the "chopstick technique" is an innovative approach that enables surgeons to simultaneously operate an endoscope, an aspirator, and a third instrument with a single hand.[20] This technique maximizes surgical efficiency and minimizes the surgical footprint, particularly in narrow intracranial corridors. Froelich's technique has been successfully applied in various neuroendoscopic procedures, including transnasal skull base surgeries, demonstrating its effectiveness and versatility.

Clinical outcomes

Clinical data consistently demonstrate the efficacy of neuroendoscopic treatment for pituitary tumors, with high resection rates, low complication rates, and improved patient outcomes. For microadenomas and functional pituitary tumors, neuroendoscopic surgery preserves endocrine function while reducing recurrencerates.[16]

Multiple studies have demonstrated that neuroendoscopic approaches achieve higher rates of GTR compared to traditional microscopic techniques. For example, a study conducted at a tertiary hospital in China reported a GTR rate of 87.9% in the neuroendoscopic group versus 66.0% in the microscopic group ($p = 0.012$).[17] Similarly, other studies have shown that neuroendoscopy facilitates more complete tumor removal, especially in large or invasive tumors, due to improved visualization and enhanced access to narrow surgical corridors.[21]

Additionally, neuroendoscopy has been associated with shorter operative times and significantly reduced intraoperative blood loss. This advantage is attributed to the precision of the instrumentation and the ability to perform surgeries through smaller incisions, minimizing tissue disruption. For instance, a comparative study found that neuroendoscopic approaches resulted in both shorter surgical durations and lower blood loss than microscopic methods.[17]

Patient-reported outcomes indicate that neuroendoscopy improves quality of life significantly. Patients who undergo neuroendoscopic pituitary tumor resection often report improvements in vision, endocrine function, and overall well-being,[14] leading to a better quality of life and a reduced psychological burden associated with the disease.

While neuroendoscopic surgery has shown superior outcomes in terms of resection rates and recovery times, challenges remain in treating large or invasive tumors. Future advancements in imaging and robotic assistance may help overcome these limitations.

Limitations and future directions

Despite its many advantages, neuroendoscopic surgery is not without limitations. One significant challenge is the steep learning curve associated with the technique,[22] requiring extensive training and experience to achieve proficiency. The confined surgical space and complex anatomy of the skull base demand exceptional hand-eye coordination and spatial awareness, which can be difficult to master. Additionally, instrument maneuverability remains a constraint, as the narrow working channels limit the range of motion and the ability to handle multiple instruments simultaneously. This limitation is particularly problematic in cases involving large or invasive tumors, where complete resection is more challenging. Another concern is the risk of cerebrospinal fluid leaks,[23] which, although reduced compared to traditional approaches, remains a potential complication, especially in extended endoscopic procedures. Furthermore, the cost of advanced neuroendoscopic equipment and the need for specialized operating room setups can be prohibitive for some healthcare institutions, limiting widespread adoption. Finally, while neuroendoscopy provides excellent visualization, standard endoscopic imaging may struggle with depth perception due to its 2D nature, potentially increasing the risk of inadvertent damage to critical structures. Addressing these limitations through technological innovation, improved training programs, and cost-effective solutions will be crucial for the continued advancement of neuroendoscopic surgery.

To overcome these challenges, future research should focus on enhancing instrument design to improve maneuverability and reduce the learning curve. The development of 3D and augmented reality visualization systems could help mitigate depth perception issues, providing surgeons with more intuitive spatial awareness. Additionally, robotic-assisted neuroendoscopy holds promise for increasing precision and reducing surgeon fatigue, particularly in complex cases. Advances in biomaterials and sealants for skull base reconstruction could further minimize the risk of cerebrospinal fluid leaks, while cost-effective neuroendoscopic systems could make the technology more accessible globally. Finally, simulation-based training programs and international collaborations could help standardize techniques and accelerate the adoption of neuroendoscopic surgery, ensuring that more patients benefit from its advantages.

Conclusions

Neuroendoscopic surgery has revolutionized the treatment of pituitary tumors, offering a minimally invasive approach with enhanced visualization, precision, and improved clinical outcomes. Despite challenges such as a steep learning curve, limited maneuverability, and the risk of cerebrospinal fluid leaks, advancements in imaging, robotics, and biomaterials hold promise for further refining the technique. Future innovations and multidisciplinary collaboration will continue to enhance the safety and efficacy of neuroendoscopic surgery, ultimately improving patient outcomes and quality of life.

Acknowledgments

None.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of interest

XJ has served as an Executive Associate Editor of *Neurosurgical Subspecialties* since July 2024. The authors declare that they have no known competing financial interests or personal relationships that could have influenced the work reported in this paper.

Author contributions

Conceptualization, methodology, investigation of this study (XH, XJ), data curation, formal analysis, writing the original draft (XH), validation, resources, and supervision (XJ). Both authors participated in the review and editing of the manuscript and approved the final version for submission.

References

[1] Daly AF, Beckers A. The Epidemiology of Pituitary Adenomas. Endocrinol Metab Clin North Am 2020;49(3):347–355. doi:10.1016/j.ecl.2020.04.002, PMID:32741475.

[2] Byun YH, Kang H, Kim YH. Advances in Pituitary Surgery. Endocrinol Metab (Seoul) 2022;37(4):608–616. doi:10.3803/EnM.2022.1546, PMID:35982611.

[3] Chavez-Herrera VR, Desai R, Gel G, Nilchian P, Schwartz TH. Endonasal endoscopic surgery for pituitary adenomas. Clin Neurol Neurosurg 2024;237:108172. doi:10.1016/j.clineuro.2024.108172, PMID:38359520.

[4] Barry S, Korbonits M. Update on the Genetics of Pituitary Tumors. Endocrinol Metab Clin North Am 2020;49(3):433–452. doi:10.1016/j.ecl.2020.05.005, PMID:32741481.

[5] Chang M, Yang C, Bao X, Wang R. Genetic and Epigenetic Causes of Pituitary Adenomas. Front Endocrinol (Lausanne) 2020;11:596554. doi:10.3389/fendo.2020.596554, PMID:33574795.

[6] Melmed S, Kaiser UB, Lopes MB, Bertherat J, Syro LV, Raverot G, *et al*. Clinical Biology of the Pituitary Adenoma. Endocr Rev 2022;43(6):1003–1037. doi:10.1210/endrev/bnac010, PMID:35395078.

[7] Landis CA, Masters SB, Spada A, Pace AM, Bourne HR, Vallar L. GTPase inhibiting mutations activate the alpha chain of Gs and stimulate adenylyl cyclase in human pituitary tumours. Nature 1989;340(6236):692–696. doi:10.1038/340692a0, PMID:2549426.

[8] Cai L, Wu ZR, Cao L, Xu JD, Lu JL, Wang CD, *et al*. ACT001 inhibits pituitary tumor growth by inducing autophagic cell death via MEK4/MAPK pathway. Acta Pharmacol Sin 2022;43(9):2386–2396. doi:10.1038/s41401-021-00856-5, PMID:35082393.

[9] Iacovazzo C, de Bonis C, Sara R, Marra A, Buonanno P, Vargas M, *et al*. Insulin-like growth factor-1 as predictive factor of difficult laryngoscopy in patients with GH-producing pituitary adenoma: A pilot study. J Clin Neurosci 2021;94:54–58. doi:10.1016/j.jocn.2021.09.021, PMID:34863462.

[10] Cui Y, Li C, Jiang Z, Zhang S, Li Q, Liu X, *et al*. Single-cell transcriptome and genome analyses of pituitary neuroendocrine tumors. Neuro Oncol 2021;23(11):1859–1871. doi:10.1093/neuonc/noab102, PMID:33908609.

[11] Zhan X, Desiderio DM. Signaling pathway networks mined from human pituitary adenoma proteomics data. BMC Med Genomics 2010;3:13. doi:10.1186/1755-8794-3-13, PMID:20426862.

[12] Chin SO. Epidemiology of Functioning Pituitary Adenomas. Endocrinol Metab (Seoul) 2020;35(2):237–242. doi:10.3803/EnM.2020.35.2.237, PMID:32615708.

[13] Ukrainets O, Guk M, Danevych O, Chukov A, Mumliev A, Solovey M, *et al*. LONG-TERM NATURAL HISTORY OF GIANT NULL CELL PITUITARY ADENOMA. Exp Oncol 2024;46(2):165–173. doi:10.15407/exp-oncology.2024.02.165, PMID:39396167.

[14] van Furth WR, de Vries F, Lobatto DJ, Kleijwegt MC, Schutte PJ, Pereira AM, *et al*. Endoscopic Surgery for Pituitary Tumors. Endocrinol Metab Clin North Am 2020;49(3):487–503. doi:10.1016/j.ecl.2020.05.011, PMID:32741484.

[15] Favier V, Le Corre M, Segnarbieux F, Rigau V, Raingeard I, Cartier C, *et al*. Endoscopic subperichondrial transseptal transsphenoidal approach is safe and efficient for non-extended pituitary surgery. Eur Arch Otorhinolaryngol 2020;277(4):1079–1087. doi:10.1007/

s00405-020-05790-6, PMID:31960129.
[16] Rahimli T, Hidayetov T, Yusifli Z, Memmedzade H, Rajabov T, Aghayev K. Endoscopic Endonasal Approach to Giant Pituitary Adenomas: Surgical Outcomes and Review of the Literature. World Neurosurg 2021;149:e1043–e1055. doi:10.1016/j.wneu.2021.01.019, PMID:33524611.
[17] Song S, Wang L, Qi Q, Wang H, Feng L. Endoscopic vs. microscopic transsphenoidal surgery outcomes in 514 nonfunctioning pituitary adenoma cases. Neurosurg Rev 2022;45(3):2375–2383. doi:10.1007/s10143-022-01732-4, PMID:35230574.
[18] Almeida JP, Gentili F. Endoscopic skull base surgery and the evolution of approaches to anterior cranial base lesions. J Neurosurg Sci 2021;65(2):101–102. doi:10.23736/S0390-5616.20.05209-1, PMID:33890753.
[19] Hahn BS, Park JY. Incorporating New Technologies to Overcome the Limitations of Endoscopic Spine Surgery: Navigation, Robotics, and Visualization. World Neurosurg 2021;145:712–721. doi:10.1016/j.wneu.2020.06.188, PMID:33348526.
[20] Serra C, Staartjes VE, Maldaner N, Holzmann D, Soyka MB, Gilone M, *et al*. Assessing the surgical outcome of the “chopsticks” technique in endoscopic transsphenoidal adenoma surgery. Neurosurg Focus 2020;48(6):E15. doi:10.3171/2020.3.FOCUS2065, PMID:32480377.
[21] Kikuchi M, Nakagawa T. Recent progress in endoscopic skull base surgery: Functional preservation and multiportal approaches. Auris Nasus Larynx 2023;50(1):32–39. doi:10.1016/j.anl.2022.04.001, PMID:35440399.
[22] Ahn Y, Lee S, Shin DW. Learning Curve for Endoscopic Transsphenoidal Surgery: A Systematic Review and Meta-Analysis. World Neurosurg 2024;181:116–124. doi:10.1016/j.wneu.2023.10.029, PMID:37838158.
[23] Cai X, Yang J, Zhu J, Tang C, Cong Z, Liu Y, *et al*. Reconstruction strategies for intraoperative CSF leak in endoscopic endonasal skull base surgery: systematic review and meta-analysis. Br J Neurosurg 2022;36(4):436–446. doi:10.1080/02688697.2020.1849548, PMID:33475004.