Int. J. Morphol.,
44(1):175-178, 2026.

Pituitary Surgery from the Pioneers to Recent Technological Innovations: What are the Key Challenges of 21st Century Surgery of the Sella Turcica?

Cirugía Hipofisaria: Desde los Pioneros hasta las Innovaciones Tecnológicas Recientes: ¿Cuáles son los Principales Desafíos de la Cirugía de la Silla Turca en el Siglo XXI?

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PALMIERI, M.; COFONE, L.; PINDINELLO, I.; ARTICO, M.; CARUBBI, C.; TAURONE, S. & SANTORO, A. Pituitary surgery from the pioneers to recent technological innovations: What are the key challenges of 21st century surgery of the sella turcica? *Int. J. Morphol., 44(1)*:175-178, 2026.

SUMMARY: Over the past two decades, surgical approaches to the sella turcica have evolved significantly, particularly with the adoption of endoscopic transsphenoidal techniques. Despite these advancements, several challenges persist, including anatomical variability, age-related morphological changes, management of large pituitary adenomas, postoperative complications, and technological limitations. This perspective article discusses these key challenges, drawing upon recent literature to highlight areas requiring ongoing research and innovation.

KEY WORDS: Sella turcica; Transsphenoidal surgery; Pituitary adenoma; Endoscopic surgery; Anatomical variability; Postoperative complications.

INTRODUCTION

The sella turcica, a saddle-shaped depression in the sphenoid bone, houses the pituitary gland and is surrounded by vital neurovascular structures such as the cavernous sinuses and the optic chiasm (Zada *et al*., 2011). The first to manifest interest in this anatomical region in the 4th century BC was Hippocrates of Cos (Cucu *et al*., 2023), who believed that the pituitary gland, from the Latin word "pituita", produced nasal mucus directly from the brain. The real function of the hypophysis remained unknown until Andreas Vesalius started to define the pituitary gland as a separate structure from the brain (Goodrich, 2000). In the following three centuries, not only were the complete functions of this gland accurately described (Pait & Arnautovic, 1997; Maartens, 2005; Dubourg *et al*., 2011), but the idea of treating tumors growing in the sella turcica surgically started to diffuse.

After the experiments on dogs by Gheorghe Marienesco (Marienesco, 1892) and Harvey Cushing (Lindholm, 2000), who proved that performing hypophysectomies is incompatible with life, the first ever attempt at transcranial surgery for a tumor involving the pituitary gland was performed by Sir Victor Horsley (Horsley, 1906), with a bilateral subfrontal approach. However, he did not succeed, as well as some contemporary surgeons like Caton (1893), who tried to remove a pituitary adenoma through a subtemporal craniotomy without being able to expose the tumor. Despite the first failed attempts, several surgeons from different countries pursued the idea of removing pituitary adenomas through transcranial routes (Cucu *et al*., 2023). Whilst the monolateral subfrontal and the subtemporal-transcavernous approaches failed the purpose, the pterional approach described by Yasargil (1984), who first proposed the transylvian route, proved to be the ideal microsurgical approach for pituitary adenomas removal.

In consideration of the anatomical relationships between the pituitary gland, the sphenoidal sinus, and the nasal fossae, at the beginning of the 19th century, Davide Giordano (Artico & Fraioli, 1998) theorized the possibility of performing a transnasal approach to the sella turcica

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Received: 2025-07-27 Accepted: 2025-11-16

region. According to Giordano's theory, W. Alfred Hirschmann performed the first ever paranasal approach to the pituitary gland (Hirschmann, 1903) with the assistance of the surgical endoscope. After this first pioneering surgical intervention, the approach was modified to reduce invasiveness and improve effectiveness: first, Haltsted (Halsted, 1910) and then Cushing (1912) proposed the sublabial incision, but the real improvement was introduced by Oskar Hirsch, who performed the first endoscope-assisted transnasal-transsphenoidal approach, which represents to date the gold-standard surgical approach for the sella turcica region (Hirsch, 1910) (Fig. 1).

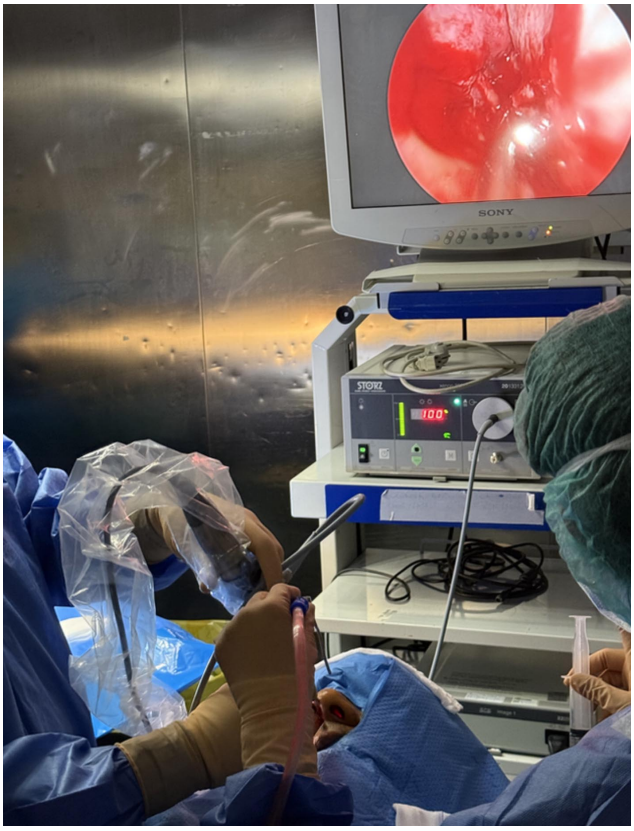

Fig. 1. Intraoperative set-up for the trans-nasalsphenoidal approach. The surgeons are positioned on either side of the patient, facing the screen. The surgical instruments are used with the dominant hand, while the other hand holds the endoscope.

As the gateway to most pituitary interventions, this anatomical site has become the focus of increasingly sophisticated surgical procedures, particularly following the advent of endoscopic transsphenoidal techniques, which offer improved visualization, less tissue disruption, and shorter recovery times. Despite these technological improvements, the sellar region continues to present complex challenges requiring tailored surgical planning, particularly due to variability in bone morphology, tumor behavior, and patient-specific anatomical constraints.

Anatomical Variability

One of the most significant and persistent challenges in sellar surgery stems from the considerable anatomical variation observed in both the sphenoid sinus and the sella turcica. These structures exhibit a wide range of differences in size, shape, pneumatization patterns, and septal configurations, all of which can critically influence the surgical corridor and the risk profile of the intervention. The degree of pneumatization of the sphenoid sinus, for instance, may range from a conchal type (non-pneumatized) to a sellar or presellar type, each presenting distinct implications for exposure. The presence of bony septations, particularly those that attach directly to the internal carotid artery (ICA) protuberances, can further complicate access and elevate the risk of vascular injury during entry. Similarly, the position and angulation of the optic nerves, cavernous sinus, and middle clinoid processes vary between individuals, occasionally demanding real-time surgical adjustments. Given these variables, meticulous preoperative radiologic evaluation is indispensable. Surgeons routinely rely on high-resolution computed tomography (CT) for bone detail and magnetic resonance imaging (MRI) for soft tissue and vascular anatomy, including the pituitary gland, tumor characteristics, and adjacent neurovascular structures. The fusion of these imaging modalities, sometimes augmented by image-guided navigation, allows for a comprehensive understanding of individual anatomy, enabling tailored surgical planning that minimizes the risk of complications such as carotid injury, optic nerve damage, or incomplete tumor resection. As highlighted by Zada *et al*. (2011), a nuanced appreciation of the neurosurgical anatomy of the sphenoid sinus and sellar floor is not merely academic, but a critical foundation for the safe and effective execution of modern endonasal approaches.

Age-Related Morphological Changes

The morphology of the sella turcica evolves dynamically across the human lifespan, with notable implications for surgical planning. In pediatric and adolescent patients, the sella is generally smaller, shallower, and more compact, often making surgical access more constrained and technically demanding. Conversely, in adults and older individuals, the sella turcica tends to expand in volume and depth, offering a broader surgical corridor but sometimes also accommodating more invasive or larger pituitary tumors. These changes are not merely dimensional but also involve the maturation of adjacent bony and neurovascular structures, which may shift in position or orientation with age. A recent high-resolution morphometric study by Sönmez *et al*. (2024) demonstrated statistically significant variations in sellar dimensions across multiple

age brackets, highlighting the necessity of age-adjusted imaging analysis, surgical trajectory planning, and instrumentation to optimize both access and safety in pituitary surgery.

Management of Large Pituitary Adenomas

Large (≥3 cm) and giant pituitary adenomas introduce considerable complexity due to their extension into adjacent structures like the cavernous sinus, optic chiasm, or suprasellar space. Achieving gross total resection without inducing hypopituitarism or vascular injury requires multistage operations, intraoperative navigation, and sometimes adjunctive radiosurgery. A classic report highlighted a 45 % gross total resection rate for large adenomas, reflecting the limits of even skilled surgical teams (Black *et al*., 1988).

Postoperative Complications

Despite substantial technical progress in endoscopic and microsurgical approaches, postoperative complications remain a major concern in sellar surgery and significantly impact patient morbidity and length of hospital stay. Among the most frequently encountered complications are cerebrospinal fluid (CSF) leaks, which can occur intraoperatively or postoperatively and are associated with an elevated risk of bacterial meningitis if not promptly recognized and managed. Additional complications include diabetes insipidus, often resulting from transient or permanent disruption of the posterior pituitary or infundibulum, as well as hematoma formation within the sellar or suprasellar space, which can compress the optic apparatus or residual gland tissue. Furthermore, anterior pituitary insufficiency may result from ischemic or mechanical injury to the gland, necessitating long-term hormonal replacement therapy. A retrospective study by El-Asmar *et al*. (2016) demonstrated that delayed recognition of CSF leaks—especially when subtle or intermittent—was associated with a significantly increased incidence of meningitis, underlining the critical role of rigorous intraoperative leak detection protocols, meticulous skull base reconstruction techniques, and close postoperative monitoring. These findings reinforce the need for interdisciplinary coordination between neurosurgeons, endocrinologists, and infectious disease specialists to ensure optimal recovery and complication management.

Technological Limitations

While endoscopic transsphenoidal techniques have largely supplanted traditional microscopic approaches as the standard of care for most sellar surgeries, they are not without significant technical and logistical limitations. One of the primary challenges is the loss of natural depth perception, as surgeons rely on two-dimensional monitor visualization rather than direct binocular vision, which can compromise spatial orientation, especially in narrow anatomical corridors. Additionally, instrument maneuverability is restricted by the confined nasal passages and narrow working channels, often necessitating specialized angled instruments and techniques that require advanced dexterity. For surgeons trained in conventional microscopic approaches, the transition to endoscopic methods presents a steep learning curve, demanding not only new psychomotor skills but also a reorientation of anatomical landmarks and intraoperative strategy. To address these limitations, recent innovations have explored incorporating augmented reality (AR), high-resolution neuronavigation systems, and robotic-assisted platforms, all of which aim to enhance precision, improve visualization, and reduce intraoperative risk (Hansasuta *et al*., 2018).

Neuronavigation systems are routinely used in neurosurgical procedures, both for cranial and spinal interventions, and pituitary surgery makes no exception [21]. Neuronavigation matches the radiological images of the patient with his real anatomy, allowing tailored approaches in each case. The infrared camera of the system detects the probe held by the operator, which is used during surgery to decide the surgical corridor, and to recognize the surrounding anatomy. The great advantage of this tool is that it prevents inappropriate exposure and the consequential injury of vital structures, above all the internal carotid artery. Moreover, the neuronavigation system is crucial for distinguishing the tumor from the normal pituitary gland. To reach this objective, the neuronavigation systems have been recently implemented with other technological tools, like the intra-operative ultrasound probes (Cabrilo *et al*., 2022) and augmented reality (Bopp *et al*., 2022; Enkaoua *et al*., 2025). Especially, the latter instrument allows the surgeon to perform a neuronavigated procedure without stopping from operating since the AR system doesn't require the use of the hand that is not holding the endoscope to use the probe of the neuronavigation system. This feature facilitates the operating workflow, reducing surgical times. Thanks to these innovative tools, pituitary surgery is becoming more effective in improving tumor resection rates, safety, and surgical comfort while operating. The introduction of new technologies in pituitary surgery is also focused on optimizing the pre-operative planning. The introduction of artificial intelligence (AI) (Maroufi *et al*., 2024) has the purpose of gathering a large amount of data to predict the ideal surgical strategy and the post-operative outcome based on patients' information, both clinical and radiological. Another tool for improving surgical planning is the creation of 3D printed models based on patients' pre-operative images [25]. The bone anatomy of the sphenoid sinus plays a pivotal role during the approach, and the

possibility of building a 3D model of the whole cranium of the patient based on his CT scan allows, in some cases, to perform mock surgeries on the artificial model to reduce complications in real-life scenarios.

However, the widespread adoption of these technologies remains constrained by several factors, including high costs, limited availability in low-resource settings, steep initial investment in training, and the need for ongoing multidisciplinary support. As technology evolves, the challenge will be to democratize access to these advanced tools while maintaining high standards of safety, training, and outcome efficacy.

CONCLUSION

Surgical interventions involving the sella turcica have benefited immensely from technological innovation in the 21st century. Yet, the region's intricate anatomy, variability with age, tumor invasiveness, and the persistent risk of complications highlight the need for continued evolution. Emphasis should be placed on patient-specific anatomical mapping, technological enhancements, and collaborative neurosurgical-endocrinological protocols to achieve safe and effective outcomes. Addressing these core challenges will define the next phase in the surgical mastery of the sellar region.

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RESUMEN: En las últimas dos décadas, los abordajes quirúrgicos de la silla turca han evolucionado significativamente, en particular con la adopción de técnicas endoscópicas transesfenoidales. A pesar de estos avances, persisten varios desafíos, como la variabilidad anatómica, los cambios morfológicos relacionados con la edad, el manejo de grandes adenomas hipofisarios, las complicaciones postoperatorias y las limitaciones tecnológicas. Este artículo de perspectiva analiza estos desafíos clave, basándose en la literatura reciente para destacar las áreas que requieren investigación e innovación continuas.

PALABRAS CLAVE: Silla turca; Cirugía transesfenoidal; Adenoma hipofisario; Cirugía endoscópica; Variabilidad anatómica; Complicaciones postoperatorias.

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