

Comparative Outcomes of Keyhole Supraorbital Approach (KSA) and Endonasal Endoscopic Transsphenoidal Approach (EETA) in Pituitary Surgery

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Background: Currently, minimal invasive surgery (the endonasal endoscopic transsphenoidal approach-EETA or keyhole supraorbital approach-KSA) is widely accepted as the best choice for pituitary tumor removal. To the best of the authors' knowledge, there is no study comparing the relative safety of these methods.

Objective: To evaluate safety and compare the complications resulting from pituitary surgery using EETA and KSA.

Material and Method: The retrospective review was performed between January 2003 and September 2013. One hundred thirty patients with pituitary adenomas were operated by using either EETA or KSA. The KSA was used on 92 cases, and the EETA was utilized on the other 38. Postoperative complications were analyzed using statistical methodologies to show statistical significance. The study was approved by the ethical committee of Rajavithi Hospital.

Results: After statistical analysis, KSA provided better outcome in term of "headache improvement" than EETA. For complications, EETA had higher incidences of unimproved vision and reoperation rate than KSA. The other major finding of the present study was that in the early year of the operations, there was higher incidence of complications. This could be associated with the level of skills of the surgeons.

Conclusion: KSA had better outcome in term of operative time, length of hospital stay, estimated blood loss, and headache improvement than EETA. For complications, EETA had higher incidence of unimproved vision and reoperation rate than KSA.

Keywords: Pituitary adenoma, Endoscope, Transsphenoid, Keyhole, Minimal invasive surgery

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Pituitary adenoma is one of the most common brain tumors. Patients present with various clinical disturbances, but hormonal abnormalities and tumor mass with compressive signs and symptoms are the most common clinical manifestations. Hormonal disturbances can be categorized into two subgroups, hormone deficit and excessive hormone secretion⁽¹⁾. Hormone deficit usually results from so-called "non-functioning" tumors, while excessive hormone secretion - as found in acromegaly, gigantism, Cushing's syndrome, or hyperprolactinemia, results from functioning tumors (hypersecretion). Available options for handling pituitary adenoma are medication, surgery, and radiosurgery. Dopamine agonist is one of the most common medications used in controlling prolactinoma^(2,3). In most cases of pituitary adenoma,

surgery seems to be the best option, especially in cases of visual deterioration due to visual pathway compression by tumor mass⁽⁴⁾.

The most common approach in pituitary surgery is the pterional approach as described by Yasargil. This approach offers surgeons a wide corridor and extra space in pituitary surgery. Tumor removal and vital structures such as the internal carotid artery, optic nerve, and chiasm, and pituitary stalk can be handled safely especially under microscopic vision. Clear 3-dimensional views can be obtained with modern microscopes, enhancing both the safety and success rates of the operation. However, the pterional approach results in more postoperative pain due to the requisite large skin incision and craniotomy flap. Patients take longer to recover after the surgery. Furthermore, total hair shaving in some cases may result in loss of confidence especially in young females. Facial asymmetry due to temporalis muscle atrophy is another detrimental side effect of this conventional approach⁽⁵⁾.

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In modern surgery, minimal invasive techniques are widely accepted in many areas of surgical specialization. The emphasis is on “small incision and less pain” and this concept seems to be readily accepted by patients. Modern neurosurgeons also apply this concept in many neurosurgical operations, and high-technology microscopes, endoscopes, coaxial microinstruments and neuro-navigators encourage neurosurgeons to adopt innovative new approaches in accordance with the minimal invasive concept^(6,7).

Minimal invasive neurosurgery can be roughly divided into two subgroups, keyhole surgery and endoscopic neurosurgery. With these techniques, neurosurgeons use smaller incision compare to that of conventional approach to delve deep into the brain with the aid of modern microscope, endoscope, and microinstruments. In some cases, endoscopes or endoscope-assisted microscopic techniques are used together. The most common keyhole approach in removing pituitary adenoma is the Keyhole Supraorbital Approach (KSA). For pure endoscopic surgery, a very small, barely visible incision will be used as a passage through which an endoscope passes deep into the brain and very close to the neurovascular structures. Neurosurgeons use the nostrils as the entry point through which the endoscope probes deep to the skull base via the sphenoidal opening. This well-known approach is called the Endonasal Endoscopic Transsphenoidal Approach (EETA).

Both of these minimal invasive techniques in pituitary adenoma surgery demand great experience, skill and practical training to minimize complications as much as possible. For inexperienced neurosurgeons, both techniques may result in devastating episodes especially massive bleeding in the surgical field. Surgery in deep narrow corridors is not easy for less experienced surgeons and may lead to many postoperative complications. The purpose of the present study was to compare the outcomes and complications between both approaches using statistical analytic tool.

Material and Method

The present research was a retrospective study conducted by reviewing pituitary adenoma patients who were treated in the Rajavithi Hospital by means of minimal invasive neurosurgery i.e. EETA or KSA. Diagnosis of pituitary adenoma was based on pathological reports, and the majority of cases were operated on by the author or in some cases with

the help of an otorhinolaryngologist between January 2003 and September 2013. Patients who had previously been operated for pituitary adenoma by other means of surgery and patients who failed to attend follow-up within six months of surgery were excluded from the present study. Of the 130 patients who were operated on, 92 were treated by KSA and 38 by EETA. In some cases of EETA, the nasal and sphenoidal phases of the surgery were conducted by an otorhinolaryngologist. In these cases, bimanual manipulation during the surgery was done by the author while endoscope handling was done by the otorhinolaryngologist. In most cases, a neuronavigator was used to ensure the position of tips of microinstruments during tumor removal. Complications from each approach were categorized as diabetes insipidus (temporary/permanent), visual problem (unimproved/deteriorated), cerebrospinal fluid (CSF) leakage, postoperative meningitis, postoperative bleeding in the surgical field, internal carotid artery injury, panhypopituitarism, hypothalamic injury, other cranial nerve injuries (excluding cranial II), approach-related complications (scar, bleeding, anosmia, nasal passage complications), reoperation, and death.

See Fig.1 for a flow chart analysis of the present study.

Statistical analysis

Descriptive statistical methods were used for describing personal characteristics by frequency, percentage, mean, and standard deviation (SD). Inferential statistical methods, with the help of SPSS version 20.0, were used to analyze the data and present as percentages and tables. Relationships between all data were analyzed using Chi-square and Fisher's exact test. Statistical significance was set at $p < 0.05$.

Results

Of the 130 patients who were diagnosed with pituitary adenoma and were operated on using minimal-invasive techniques, 92 were operated by KSA and 38 by EETA. The average age of the population studied was 43.2 years, and the majority of patients (64.7%) were female. The majority of adenomas (75.3%) were classified as macroadenoma (maximum diameter >10 mm). Total removal achieved by KSA was 83%, while EETA showed 76%. The average duration of hospital stay was 5.5 days in the KSA group and 7.2 days in the EETA group. More details of patient demographic data were shown in Table 1.

The most common clinical manifestations that resulted in patients seeking treatment were visual deterioration (77%), followed by headache from increased intracranial pressure (64%), nausea and vomiting (30%), and hormonal disturbance symptoms (22%). More details of clinical manifestations were shown in Fig.2.

In both approaches, diabetes insipidus (DI) was the most common complication. Most of the

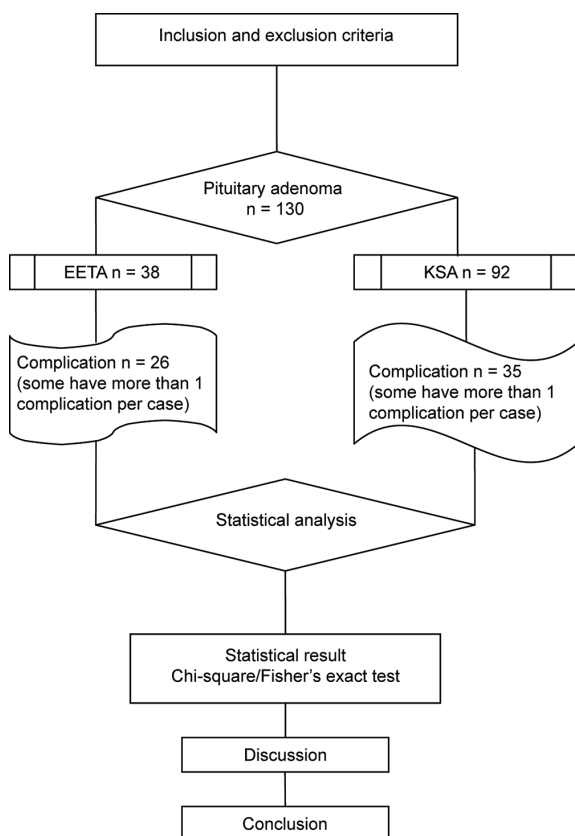


Fig. 1 Protocol flow chart.

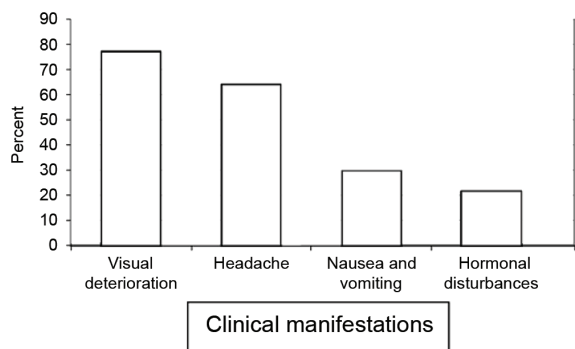


Fig. 2 Most common clinical manifestations.

Table 1. Demographic data

Variable	Total (n = 130)	
	n	%
Age at diagnosis (years)		
Younger than 30	19	14.6
30-39	27	20.7
40-49	46	35.3
50-59	25	19.2
Older than 60	13	10.2
Median age	43.2	
Tumor extension beyond sella (%)		
None	25	19.2
Yes	105	80.8
Gender		
Male	46	35.3
Female	84	64.7
Tumor size (%)		
Macroadenoma (>10 mm)	98	75.3
Microadenoma (<10 mm)	32	24.6

incidences were temporary DI (20 out of 24 patients). One death occurred in EETA due to major vessel (internal carotid artery) injury. Although bleeding was controlled intraoperatively, death still occurred due to severe postoperative vasospasm. However, this serious mortality complication occurred only in the early phase of the surgery, and after a high learning curve was achieved, no more serious complications occurred. Table 2 and 3 shows characteristics of study subjects, outcomes, and complications respectively.

There were significant differences in operative time, length of hospital stay, and estimated blood loss between KSA and EETA groups. In other word, KSA showed better result in operative time, length of hospital stay, and estimated blood loss than in EETA (Table 2).

From statistical analysis tool as shown in Table 3, both EETA and KSA showed no statistically significant differences in alleviation preoperative symptoms except for the headache that KSA was superior to EETA, ($p < 0.001$).

Cerebrospinal fluid (CSF) leakage was found in both approaches. The authors noted that the incidence of CSF leakage after KSA was higher in the first few years of practice, while for EETA, the incidence seemed to be more random.

Statistical analysis showed that there were two significant complications between both approach, unimproved vision ($p = 0.01$) and reoperation ($p = 0.03$) (as shown in Table 3).

Table 2. Characteristics of study subjects

Variable	KSA	EETA	<i>p</i> -value
Number of subjects	92	38	
Average operative time (min)	56.80±15.49	118.29±64.50	<0.001*
Average length of hospital stay (day)	5.49±2.05	7.24±2.84	<0.001*
Average estimated blood loss (ml)	269.82±116.29	489.87±436.33	0.004*

KSA = keyhole supraorbital approach; EETA = endonasal endoscopic transsphenoidal approach

Values are mean ± standard deviation, otherwise is specified

* *p*<0.05

Table 3. Outcome and complication

Outcome and complication	Operative technique		<i>p</i> -value
	KSA, n (%) (total n = 92)	EETA, n (%) (total n = 38)	
Total removal	76/92 (82.6)	28/38 (73.7)	0.249
Visual improvement	70/71 (98.6)	27/30 (90.0)	0.550
Hormonal improvement	18/20 (90.0)	6/6 (100)	0.615
Improvement of headache	65/75 (86.7)	14/19 (73.7)	<0.001
Diabetes insipidus			
Temporary	15 (16.3)	5 (13.2)	0.65
Permanent	4 (4.3)	0 (0.0)	0.19
Vision problem			
Unimproved	0 (0.0)	3 (7.9)	0.01*
Deterioration	1 (1.1)	0 (0.0)	0.51
Cerebrospinal fluid leakage	4 (4.3)	4 (10.6)	0.18
Meningitis	1 (1.1)	0 (0.0)	0.51
Postoperative bleeding	1 (1.1)	0 (0.0)	0.51
Internal carotid artery injury	0 (0.0)	1 (2.6)	0.11
Panhypopituitarism	2 (2.2)	0 (0.0)	0.36
Hypothalamic injury	0 (0.0)	1 (2.6)	0.11
Cranial nerve injuries (exclude CN II)	1 (1.1)	2 (5.3)	0.14
Approach related complications (e.g. anosmia, scar, nasal complication)	4 (4.3)	5 (13.2)	0.07
Reoperation	2 (2.2)	4 (10.5)	0.03*
Death	0 (0.0)	1 (2.6)	0.29

* *p*<0.05

The authors also noted that serious and fatal complications such as internal carotid injury, hypothalamic damage, and cranial nerve palsies, in both approaches occurred most within the first two years of the operations.

Discussion

Nowadays, there are only two approaches (KSA and EETA) to minimal invasive concept in pituitary tumor surgery. Many articles were published about the pros and cons of both approaches.

Cappabianca et al⁽⁸⁾ summarized EETA into three consecutive phases, the nasal, sphenoid, and sellar phases. Unlike the traditional transseptal transsphenoidal approach, there is no use of transsphenoidal retractor. Therefore, in EETA, there is no destruction of nasal septum, which is the main cause of postoperative nasal deformity and discomfort. The most critical stages are the sphenoid and sellar phases in which surgeons have to identify many important landmarks especially the carotid prominence. Failure to identify the prominence might cause internal carotid

injury, which is potentially fatal. In the study by Hofstetter et al⁽⁹⁾, total pituitary adenoma removal using EETA was achieved up to 75.6% of cases. They found that lower rates of cure occurred in growth hormone (GH)-secreting macroadenomas due to a high rate of cavernous sinus invasion, and in adrenocorticotropic (ACTH)-secreting adenomas due to a high rate of lesions that were not visible on preoperative MR imaging. While univariate analysis showed that macroadenoma, suprasellar, cavernous extension, and extent of resection correlated with cure, multivariate analysis showed that only extent of resection and suprasellar extension were predictor of cure. In their study, only a few patients developed postoperative panhypopituitarism and CSF leakage. In the large series study by Arbolay et al⁽¹⁰⁾, 278 pituitary adenomas were operated using EETA, and total removal was achieved in 92.4%. The most common complication was CSF leakage, which was encountered more frequently in cases of macroadenomas with extensive suprasellar extension requiring opening of the subarachnoid space during the dissection. They stressed that watertight repair by different techniques especially the nasoseptal flap is mandatory. Permanent diabetes insipidus occurred in 11 patients, while four patients developed panhypopituitarism postoperatively. Santos et al⁽¹¹⁾ reported 30 cases of pituitary adenoma patients. The removal was achieved using KSA. Three patients had diabetes insipidus (2 permanent) and five had CSF leakage treated with lumbar drainage.

Wiedemayer et al⁽¹²⁾ reported an evaluation of KSA and its indications, advantages, and limitations. They concluded that KSA was safe, effective and time-sparing. Ormond et al⁽¹³⁾ had reviewed the evolution of KSA and stressed that KSA played a legitimate role in the armamentarium of the modern skull base surgeon, offering a less invasive but still efficacious approach to a number of lesions along the subfrontal corridor. For newcomers who do not have enough experience and need more practical experience, a smaller, simpler lesion should be performed first before moving on to larger, more complicated ones. They suggested that midline and suprasellar lesions were more easily accessed through this approach than laterally-based lesions. The present study showed similar result to those reported by Zheng et al⁽¹⁴⁾. However, in Zheng's study, an endoscope was used to assist the microscope via a keyhole incision. Complications such as diabetes insipidus and subcutaneous edema occurred in few patients, but they all made spontaneous recovery.

The paper by Fatemi et al⁽¹⁵⁾ applied both EETA and KSA for non-pituitary adenoma patients. In their study, they operated 44 craniopharyngioma and meningioma patients. They found that the endonasal route was preferred for removal of most retrochiasmal craniopharyngiomas, whereas the supraorbital route was recommended for meningiomas larger than 30 to 35 mm or with growth beyond the supraclinoid carotid arteries. For smaller midline tumors, either approach could be used, depending on surgeon experience and tumor anatomy. In "Advances in endoscopic surgery" by Emmanuel et al⁽¹⁶⁾, EETA seemed to be less invasive than KSA. The endonasal routes offered genuine benefits for pituitary surgery as well as for retrochiasmatic or midline clival tumors. However, the keyhole supraorbital route seemed suitable for tumors with more lateral extension. CSF leakage after tumor removal also occurred less frequently in KSA.

The result of the present study are in agreement with previously mentioned articles that even though minimal invasive surgery plays an important role in modern neurosurgery, both KSA and EETA still carry some risks. The most common postoperative complications, DI and CSF leakage, were the same as those found in the above articles. However, there were two statistical significances in terms of complications between both approaches. After statistical analysis tool, unimproved vision ($p = 0.01$) and reoperation rate ($p = 0.03$) were higher in EETA than in KSA. For outcome, KSA resulted in better improvement of headache than in EETA ($p < 0.001$).

Most of the complications occurred in the first few years of the studies. These finding should be related with the experience of the surgeons. It should be stressed that both approaches demand a high learning curve. Surgery under narrow and deep corridors can be fatal if neurosurgeons do not have sufficient experience or are working without supervision from experienced mentors.

Conclusion

Although minimal-invasive techniques for pituitary adenomas removal are effective and less invasive than the conventional approach, they are not risk-free operations. Many factors, especially the expertise of neurosurgeons play an important role in these operations. From the present study, KSA had better outcome in term of operative time, length of hospital stay, estimated blood loss, and headache improvement than EETA. EETA had higher incidences of unimproved vision and reoperation rate than KSA.

What is already known on this topic?

Minimal invasive neurosurgical procedures for pituitary tumor removal are classified as Keyhole Supraorbital Approach (KSA) and Endoscopic Endonasal Transsphenoidal Approach (EETA). Unlike the conventional way to visualize neurovascular structures, with the use of microscopes in KSA, whereas the use of endoscope in EETA, both methods use a small passage to reach into the deep part of the brain and close to critical neurovascular structures. They are less invasive and patients have fewer complications, less pain, satisfying cosmetic result, and faster recovery times.

Pituitary tumor surgery can be done by either procedures based on the surgeon and patient agreement. The KSA is simpler, require less learning curve and offer a better exposure to manage serious complications especially severe bleeding. With EETA, there is no external scar but surgeon needs more skill and meticulous knowledge of the ventral skull base anatomy. There are many articles discussed about pros and cons of each approach, but none had compared the outcomes and complications.

What this study adds?

Even with major improvement of technology and surgical equipment, both approaches have disadvantages in term of the outcome and complications. The present study showed statistical significance ($p < 0.001$) of postoperative headache improvement in KSA group, while EETA showed higher incidence (with statistical significance) of unimproved vision ($p = 0.01$) and reoperative rate ($p = 0.03$). The present study also revealed that the complications in EETA group were higher in the first few years of practice, so EETA might demand more learning curve than in KSA.

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Potential conflicts of interest

None.

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การศึกษาเปรียบเทียบผลการผ่าตัดเนื้องอกต่อมใต้สมองด้วยวิธีการผ่าตัดแผลเล็กแบบรูกุญแจบริเวณเหนือกระดูกอกตากับการผ่าตัดผ่านกล้องทางรูจมูก

เมธี วงศ์ศิริสุวรรณ, กฤษณี กาญจนพันธ์ุ

ภูมิหลัง: ในปัจจุบันการผ่าตัดเนื้องอกต่อมใต้สมองแบบ “แผลเล็ก เจ็บน้อย” (การผ่าตัดผ่านกล้องทางรูจมูก และการผ่าตัดแผลเล็กแบบรูกุญแจบริเวณเหนือกระดูกอกตา) ถือว่าเป็นการผ่าตัดที่ดีที่สุดสำหรับผู้ป่วย แม้ว่าจะมีรายงานการผ่าตัดมากมาด้วยสองวิธีดังกล่าว แต่ยังไม่พบว่ามีการเปรียบเทียบความแตกต่างในประเด็นเรื่องผลการรักษาของทั้งสองวิธี

วัตถุประสงค์: ศึกษาเปรียบเทียบผลการผ่าตัดและภาวะแทรกซ้อนของการผ่าตัดเนื้องอกต่อมใต้สมองด้วยวิธีการผ่าตัดผ่านกล้องทางรูจมูก (EETA) กับวิธีการผ่าตัดแผลเล็กแบบรูกุญแจเหนือกระดูกอกตา (KSA)

วัสดุและวิธีการ: คณะผู้นิพนธ์ได้เก็บรวบรวมข้อมูลย้อนหลังของกลุ่มตัวอย่างประกอบด้วยผู้ป่วยเนื้องอกต่อมใต้สมองที่ได้รับการผ่าตัดแผลเล็กแบบรูกุญแจบริเวณเหนือกระดูกอกตากับการผ่าตัดผ่านกล้องทางรูจมูกในระหว่างเดือนมกราคม พ.ศ. 2546 ถึง เดือนกันยายน พ.ศ. 2556 จำนวนทั้งสิ้น 130 ราย ในจำนวนนี้ 92 ราย ได้รับการผ่าตัดด้วยวิธี KSA และอีก 38 ราย ได้รับการผ่าตัดด้วยวิธี EETA ภาวะแทรกซ้อนที่เกิดขึ้นได้ถูกนำมาแจกแจงและคำนวณหาความแตกต่างที่เกิดขึ้นว่ามีนัยสำคัญทางสถิติหรือไม่ด้วยเครื่องมือทางสถิติตามระเบียบวิธีการศึกษา ทั้งนี้การศึกษานี้ได้รับการรับรองตามขั้นตอนของคณะกรรมการจริยธรรมของโรงพยาบาลราชวิถี

ผลการศึกษา: จากการคำนวณทางสถิติพบว่า การผ่าตัดแผลเล็กแบบรูกุญแจบริเวณเหนือกระดูกอกตาได้ผลดีกว่าแบบผ่านกล้องทางรูจมูกในแง่ของอาการปวดศีรษะที่ดีขึ้นมากกว่า ส่วนภาวะแทรกซ้อนนั้น การผ่าตัดผ่านกล้องทางรูจมูกมีอัตราการเกิดปัญหาเรื่องสายตาที่ไม่ดีขึ้นหลังผ่าตัด และอัตราการผ่าตัดซ้ำสูงกว่าการผ่าตัดแผลเล็กแบบรูกุญแจบริเวณเหนือกระดูกอกตา นอกจากนี้ยังพบว่าภาวะแทรกซ้อนของการผ่าตัดมักเกิดขึ้นในช่วงสองสามปีแรกนับแต่เริ่มทำการผ่าตัด หลังจากนั้นจะค่อยๆ ลดลง ซึ่งน่าจะเกิดจากประสบการณ์ที่มากขึ้นของศัลยแพทย์

สรุป: การผ่าตัดแบบแผลเล็กแบบรูกุญแจบริเวณเหนือกระดูกอกตาให้ผลดีกว่าการผ่าตัดผ่านทางรูจมูกด้วยกล้องในแง่ของระยะเวลาการผ่าตัด ระยะเวลาการนอนโรงพยาบาล จำนวนการเสียเลือด และยังช่วยให้อาการปวดศีรษะดีขึ้นมากกว่าการผ่าตัดผ่านทางรูจมูกด้วยกล้อง นอกจากนี้การผ่าตัดผ่านทางรูจมูกด้วยกล้องจะมีอัตราการนำผู้ป่วยมาผ่าตัดซ้ำ รวมทั้งพบปัญหาสายตาไม่ดีขึ้นหลังการผ่าตัดสูงกว่าการผ่าตัดแบบแผลเล็กแบบรูกุญแจบริเวณเหนือกระดูกอกตา
