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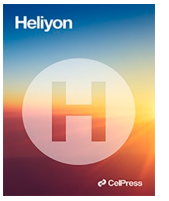

Research article

The key point of transsphenoidal surgery for infradiaphragmatic craniopharyngioma : Better sellar diaphragm resection

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ABSTRACT

Background: Craniopharyngiomas have a high recurrence rate and a poor prognosis, and the key methods for reducing recurrences are unknown. The aim of this study was to explore the key points of microscopic or endoscopic transsphenoidal surgery used to treat infradiaphragmatic craniopharyngiomas.

Methods: We reviewed the medical records of patients with infradiaphragmatic craniopharyngiomas who were admitted to Peking Union Medical College Hospital between 2011 and 2018.

Results: When considering tumor location, all 34 patients had intrasellar tumors, with 19 of them exhibiting suprasellar extensions. Of the 34 patients, 24 patients underwent resection under the microscope and the remaining 10 patients underwent transsphenoidal endoscopic surgery. Gross total tumor resection was achieved in 16 patients. Twelve patients underwent invaded sellar diaphragm resection, while the remaining 22 patients were not. Cerebrospinal fluid leaks occurred during surgery in 18 patients. Visual acuity improved in two patients. After an average follow-up of 31.1 months, 13 patients experienced tumor recurrence. The short term recurrence rate in the sellar diaphragm resection group was significantly lower compared to the non-resected group ($P < 0.001$). Moreover, based on distinct surgical methods, the endoscope group displayed a reduced short term recurrence rate compared to the microscope group ($P = 0.0048$).

Conclusion: Invaded sellar diaphragm resection emerges as a pivotal maneuver in craniopharyngioma surgery, substantively influencing tumor recurrence. Capitalizing on the advantageous angled lens of endoscopes, surgeons can achieve heightened visualization. Significantly, the endoscopic approach exhibits a superior capacity to curtail recurrence, while effectively managing potential complications, when contrasted with the microscope group.

1. Background

Craniopharyngioma is a low-grade epithelial tumor with an annual incidence of about 0.5–2.0 patients/million/year [1], and its benign histological characteristic may conceal its biological behavior. The symptoms are closely related to the critical structures it involves [2], in particular the optic chiasm, hypothalamus, pituitary stalk, and vessels in the circle of Willis [3,4]. Based on its

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relationship with the sellar diaphragm and the third ventricle, craniopharyngiomas can be divided into different subtypes. Among them, intrasellar craniopharyngioma is unique as its location makes it possible to resect it completely via transsphenoidal surgery and with fewer complications. However, the symptoms of intrasellar craniopharyngioma are more severe than other types because of its close relationship with surrounding structures. It is also not uncommon for clinical surgeons to misdiagnose this type of tumor as a pituitary adenoma. In terms of ideal surgical approaches, endoscopic surgery has unique advantages compared with surgery performed under the microscope. Because of the changeable viewing angle of the endoscope, endoscopic surgery allows better surgical visualization of the suprasellar area and avoids impairing important structures during the procedure [5]. Postoperative complications such as cerebrospinal fluid (CSF) leakage and long-term hypopituitarism occur more frequently in patients with intrasellar craniopharyngioma compared with those with pituitary adenomas. The chance of recurrence often depends on the amount of adhesion between the tumor and surrounding tissues, especially the sellar diaphragm, as well as the proficiency of the surgeon and the surgical approach taken. Unsuccessful resection of the invaded sellar diaphragm is considered to be closely related to recurrence. The broader view of the sellar diaphragm provided by endoscopy may permit better resection of the invaded sellar diaphragm and reduce recurrence rates. We investigated the key points of transsphenoidal surgery used to treat infradiaphragmatic craniopharyngiomas and discovered that resection of the sellar diaphragm is critical in craniopharyngioma removal surgery and is associated with tumor recurrence.

2. Materials and methods

The 34 patients in this study were treated at the Department of Neurosurgery in Peking Union Medical College Hospital (PUMCH) between 2011 and 2018. The selection criteria were: 1. Preoperative imaging that indicated the tumor was located in the infradiaphragmatic area (Fig. 1), 2. Postoperative histology that confirmed craniopharyngioma, and 3. The first time the patient had undergone pituitary surgery. This study was approved by the Ethics Committee of Peking Union Medical College Hospital (ID: I-24PJ1197), and all patients involved signed a written informed consent form.

After admission, we conducted detailed medical history collection, a physical examination, and enhanced pituitary magnetic resonance image (MRI) for each patient. All patients received neuroendocrinological evaluations before and after surgery. All patients received one of two types of surgery: endoscopic transsphenoidal surgery or microscopic transsphenoidal surgery. The follow-up interval was 3 months, 6 months, and 12 months after surgery, and then every 6 months thereafter. Follow-up parameters included the patient's quality of life, hormone levels, and presence or absence of recurrence.

Our definition of sellar diaphragm resection involves surgically removing the parts of the sellar diaphragm that have been invaded by the tumor during the operation.

Technique used to close the CSF leak: The first step is to place an artificial dura mater for isolation. If the operating space allows, the dura can be sutured to the autologous fascia. The second step involves filling with autologous fat. The third step is to cover the autologous fat with the patient's own fascia, such as fascia from the quadriceps muscle of the lower limb. If the surgery is performed endoscopically, the enhanced visibility allows for further reinforcement and suturing of a pedicled nasal septal mucosal flap with the quadriceps fascia.

Data in this study were collected with Microsoft Excel (2022), and were presented in the form of mean ± standard deviation or as median. Data analyses were performed with SPSS 13.0 statistical software (IBM, Armonk, NY).

3. Results

3.1. Preoperative imaging

When considering tumor location, all 34 patients had intrasellar tumors, with 19 of them exhibiting suprasellar extensions. Tumor compositions varied, with cystic, solid, and mixed types noted, along with calcifications in four cases.

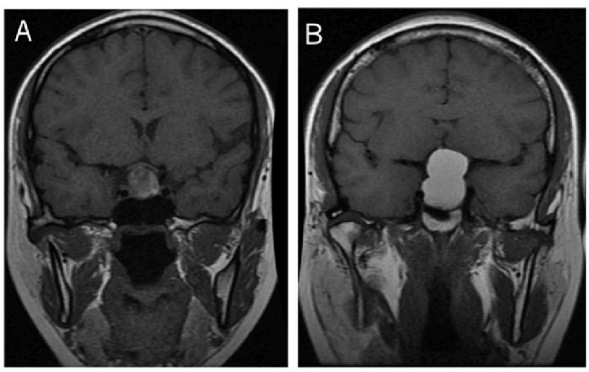

Fig. 1. The MRI images delineate the tumor's location. Image A is characterized by the tumor's intrasellar positioning, while Image B defines its location as intrasuprasellar.

3.2. Intraoperative situation

Surgical interventions included sellar diaphragm resection in 12 patients and endoscopic or microscope-assisted procedures in others. Gross total resection (GTR) was achieved in 25 patients, and subtotal resection in 9. Intraoperative cerebrospinal fluid leaks were noted in 18 patients, all undergoing sellar diaphragm resection.

3.3. Pathology

The histopathological analysis of the tumors in all 34 patients confirmed craniopharyngiomas, of which two patients were classified as squamous epidermal type, three patients were ameloblastic type, and the rest were not classified.

3.4. Follow up

Thirty-one patients are still being monitored while the remaining three were lost to follow-up. The follow-up period ranged from 3 months to 132 months (average 31.1 months). Four patients with hormonal disorders had hormone levels return to normal post-operatively, while 12 patients required hormone replacement therapy (HRT) after surgery (Table 3). The recurrence rate in the sellar diaphragm resection group was significantly lower compared to the non-resected group ($P < 0.001$) (Table 1). Moreover, based on distinct surgical methods, the endoscopic group displayed a reduced recurrence rate compared to the microscope group ($P = 0.0048$) (Table 2).

The following Fig. 2 (A-J) shows MR images from patient 27, who underwent transsphenoidal endoscopic surgery and sellar diaphragm resection. During the follow-up period of 51 months, there was no evidence suggesting recurrence.

4. Discussion

Craniopharyngioma is a rare embryonic malformation arising from the squamous epithelial remnants of Rathke's pouch. There are many ways to classify craniopharyngiomas. In terms of location, they can be divided into three types based on their relationship to the sellar region (Fig. 2): 1) suprasellar craniopharyngiomas, 2) intra- and suprasellar craniopharyngiomas, and 3) purely intrasellar craniopharyngiomas [6]. Infradiaphragmatic craniopharyngiomas are relatively rare compared with the supradiaphragmatic type and account for approximately 5 % of patients [7]. In this study, all 34 patients had intrasellar tumors, with 19 of them exhibiting suprasellar extensions. When the tumor invades and gradually impinges on the sellar region, patients develop visual disorders. Infradiaphragmatic craniopharyngiomas can induce more severe symptoms compared with supradiaphragmatic craniopharyngiomas, including signs of endocrine dysfunction and visual disturbances, because of the compression of the pituitary gland and surrounding structures.

Transsphenoidal surgery can provide a clearer and wider vision of the surgical field with fewer complications compared with transcranial surgery [8,9]. Wang et al. suggest that, though transsphenoidal surgery may impair the pituitary gland, it has great advantages in improving hyperprolactinemia and alleviating visual impairment and defects. At the same time, it is associated with a low recurrence rate [7]. Almeida JP et al. [10] conducted a review and analysis of previous studies. Their findings indicated that Endoscopic transsphenoidal surgery had a higher rate of GTR than open methods (90 % vs. 40 %, $P = 0.009$). Additionally, this approach resulted in better visual recovery (63 % vs. 0 %, $P < 0.05$) and reduced the incidence of complications (20 % vs. 80 %, $P < 0.001$).

Endoscopic transsphenoidal surgery has become a reliable treatment method for primary and recurrent craniopharyngiomas in the last decade [11]. For infradiaphragmatic craniopharyngiomas that originate from the pituitary stalk, endoscopic surgery is an efficient way to dissect the adhering and surrounding vital structures. According to a retrospective study of 226 patients [12], intrasellar craniopharyngiomas carry the lowest probability of hypothalamic dysfunction after radical resection compared with the other types of craniopharyngiomas. Over the last decade, neurosurgeon preference for endoscopy has increased significantly [13]. The most obvious advantage of endoscopic surgery is providing a panoramic view of the operating field with changeable angles, especially in the suprasellar area, which allows surgeons to obtain a precise view of the surrounding critical structures [5,14,15]. With the help of

Table 1
Surgical complications: Classified by whether the invaded sellar diaphragm was resected or not.

Resection of the sellar diaphragm	Yes (12)	No (22)	P value
Intraoperative CSF Leakage	12	6	<0.001
Intracranial infections	1	0	0.3529
Newly occurred short-term diabetes insipidus	7	5	0.0619
Long-term diabetes insipidus	2	4	>0.9999
Newly occurred central hypothyroidism	2	6	0.6809
Gross total removal	12	14	0.03036
Recurrence[a]	0	13	**<0.001**
Hormone replace therapy	4	8	>0.9999

$P < 0.05$ was considered statistically significant.
[a] Incomplete surgical resection of the tumor was also classified as recurrent patient.

Table 2
Surgical complications: Classified by surgery approaches.

	Endoscopic (10)	Microscopic (24)	P value
Intraoperative CSF Leakage	10	9	<0.001
Intracranial infections	1	0	0.2941
Newly occurred short-term diabetes insipidus	6	6	0.1122
Long-term diabetes insipidus	2	4	>0.9999
Newly occurred central hypothyroidism	2	6	>0.9999
Gross total removal	10	16	0.0720
Recurrence[a]	0	13	**0.0048**
Hormone replace therapy	3	9	>0.9999

$P < 0.05$ was considered statistically significant.
[a] Incomplete surgical resection of the tumor was also classified as recurrent patient.

angled lens endoscopes, surgeons can even obtain direct visualization of the suprasellar region [16]. This better visualization allows the normal pituitary tissue to be more easily distinguished from the cystic walls of the tumor and better invaded sellar diaphragm resection can be achieved without the need to blindly rely on surgeon experience. In our study, 12 patients underwent sellar diaphragm resection, while the remaining 22 patients were not. In terms of average GTR rate, the resection group was 100 %, while the other group was 63.6 % ($P = 0.030$). However, there was significant difference in the short term recurrence rate between the two groups (0 % vs 59.1 %, $P < 0.001$). Within the study group, 10 patients underwent endoscopic surgery, while the remaining 24 patients underwent procedures with microscope assistance. Notably, the endoscopic group exhibited a notably diminished recurrence rate in comparison to the microscope group ($P = 0.0048$).

In this study, we observed that the postoperative complications stemming from the two surgical approaches did not exhibit significant differences (with the exception of CSF leakage, as documented in Tables 1 and 2). Thus, as the goal is to remove as much of the tumor as possible to reduce the recurrence rate, better sellar diaphragm resection is recommended. Intraoperative CSF leakage occurred in 100 % of patients in the sellar diaphragm resection group, while the rate within the sellar diaphragm reservation group was 31.8 % ($P < 0.001$). However, even if the probability of cerebrospinal fluid leakage increases, this is likely an acceptable cost given the decreased risk of tumor recurrence and that the leakage can be addressed with fascia lata, muscle, or fat implantation [17]. In addition, there was only one patient with CSF leakage develop intracranial infections. According to a prospective, multicenter, controlled research study of nonfunctioning pituitary adenomas, less experienced endoscopic surgeons can surprisingly achieve similar GTR rates compared with experienced microscopic surgeons [18]. Endoscopic surgery has less of a learning curve and it is easier for less experienced surgeons to achieve good results in a shorter time. This study [18] also found that in experienced hands, endoscopic surgery carries a low complication rate, which was consistent with our results.

If it is impossible to completely remove tumors or if gross resection may result in severe side effects, then postoperative radiation can be considered to improve the prognosis [19–22]. Recent research has proven that limited surgery and photon-based conformal radiation therapy achieve excellent tumor control [23]. For cystic craniopharyngiomas, [32P] intracavitary irradiation is recommended [24].

5. Conclusion

The key to successful microscopic or endoscopic transsphenoidal surgery for infradiaphragmatic craniopharyngiomas lies in invaded sellar diaphragm resection. Due to the recurrence risk associated with craniopharyngiomas, a gross complete resection is crucial for both patients and surgeons. In this research, the invaded sellar diaphragm resection group had lower recurrence rates than the protect group, and the complications were not excessive. With the advancement of repair technology, CSF leakage induced by total resection of the sellar diaphragm will be better healed. Endoscopes can provide a panoramic view of the operative field and have a shorter learning curve than microscopes. In light of this, they may eventually play a pivotal role in the surgical treatment of infradiaphragmatic craniopharyngiomas.

Declarations

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Ethics approval and consent to participate

Informed consent was obtained from all individual participants or their parents and/or legal guardians included in the study. This retrospective study was approved by the Ethics Research Board of Peking Union Medical College Hospital (PUMCH). All experiments and methods were performed in accordance with relevant guidelines and regulations.

Table 3
Clinical data of 34 patients with infradiaphragmatic craniopharyngioma.

patients	Age /sex	Tumor location	Surgery	Resection of invaded sellar diaphragm	Intraoperative CSF Leakage	Tumor resection	Follow-Up (months)	Recurrence	HRT
1	13/M	Intrasuprasellar	microscope	No	No	GTR	24	No	Yes
2	34/F	Intrasellar	microscope	No	Yes	GTR	3	No	No
3	35/F	Intrasuprasellar	microscope	No	No	GTR	60	No	No
4	34/F	Intrasellar	microscope	No	No	GTR	24	No	No
5	27/M	Intrasellar	microscope	No	No	GTR	24	No	No
6	42/F	Intrasuprasellar	microscope	Yes	Yes	GTR	36	No	Yes
7	41/F	Intrasellar	microscope	Yes	Yes	GTR	8	No	No
8	8/F	Intrasuprasellar	microscope	No	No	GTR	6	No	Yes
9	65/M	Intrasellar	microscope	No	Yes	GTR	10	Yes	Yes
10	45/F	Intrasuprasellar	microscope	No	Yes	GTR	16	Yes	No
11	30/F	Intrasellar	microscope	No	Yes	GTR	106	No	Yes
12	24/M	Intrasuprasellar	microscope	No	Yes	GTR	17	Yes	Yes
13	22/F	Intrasellar	microscope	No	Yes	GTR	12	No	No
14	26/F	Intrasuprasellar	microscope	No	No	GTR	12	Yes	Yes
15	21/F	Intrasellar	microscope	No	No	GTR	24	No	ND
16	22/M	Intrasuprasellar	microscope	No	Yes	GTR	44	Yes	Yes
17	10/M	Intrasuprasellar	microscope	No	No	STR	36	Yes	Yes
18	30/F	Intrasellar	microscope	No	No	STR	13	Yes	No
19	56/F	Intrasuprasellar	microscope	No	No	STR	5	Yes	No
20	36/F	Intrasellar	microscope	No	No	STR	3	Yes	ND
21	37/F	Intrasuprasellar	microscope	No	No	STR	18	Yes	No
22	66/F	Intrasuprasellar	microscope	No	No	STR	12	Yes	No
23	15/F	Intrasuprasellar	microscope	No	No	STR	54	Yes	ND
24	53/F	Intrasuprasellar	microscope	No	No	STR	3	Yes	ND
25	4/F	Intrasuprasellar	endoscope	Yes	Yes	GTR	120	No	Yes
26	24/M	Intrasellar	endoscope	Yes	Yes	GTR	60	No	Yes
27	24/F	Intrasuprasellar	endoscope	Yes	Yes	GTR	54	No	No
28	21/F	Intrasellar	endoscope	Yes	Yes	GTR	3	No	ND
29	14/M	Intrasellar	endoscope	Yes	Yes	GTR	12	No	No
30	38/M	Intrasuprasellar	endoscope	Yes	Yes	GTR	48	No	No
31	14/M	Intrasellar	endoscope	Yes	Yes	GTR	32	No	No
32	44/M	Intrasellar	endoscope	Yes	Yes	GTR	22	No	No
33	17/F	Intrasuprasellar	endoscope	Yes	Yes	GTR	132	No	Yes
34	6/M	Intrasuprasellar	endoscope	Yes	Yes	GTR	3	No	No

HRT hormone replace therapy; *M* male; F female; *GTR* gross total removal; *STR* Subtotal resection; *ND* not determined.

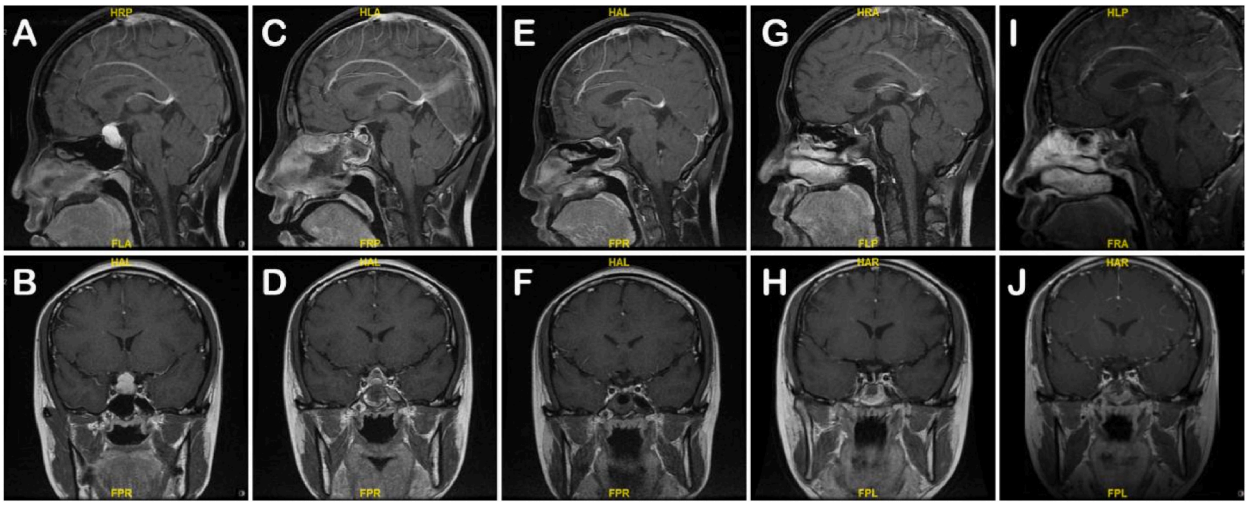

Fig. 2. MRI obtained from patient 27, who received transsphenoidal endoscopic surgery and sellar diaphragm resection. (**AB**) Preoperative coronal and sagittal T1-weighted with contrast MR images showed high signal intensity and a snowman-like appearance in the intrasuprasellar region. Coronal and sagittal T1-weighted with contrast MR images 5 days (**CD**), 6 months (**EF**), 36 months (**GH**), and 51 months (**IJ**) after surgery showed no recurrence.

Consent to publish

Patients signed informed consent regarding publishing their data.

Data availability statement

The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

CRediT authorship contribution statement

Qi Liu: Writing – original draft. **Xiaokun Chen:** Writing – original draft. **Xinjie Bao:** Writing – review & editing, Funding acquisition, Conceptualization. **Yong Yao:** Writing – review & editing, Resources. **Kan Deng:** Resources. **Ming Feng:** Resources. **Wei Lian:** Resources. **Bing Xing:** Conceptualization. **Renzhi Wang:** Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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