Investigating the application of diving endoscopic technique in determining the extent of pituitary adenoma resection via the trans-nasal-sphenoidal approach

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Abstract. The aim of the present study was to investigate the advantages and disadvantages of the diving endoscopic technique in pituitary adenoma surgery, and the application value in determining the extent of tumor resection. A total of 37 patients with pituitary adenoma initially underwent tumor resection under an endoscope-assisted microscope via standard trans-nasal-sphenoidal approach, and tumor cavity structure was observed by applying the diving endoscopic technique. Surgery was subsequently performed again under a microscope or endoscope. The diving endoscopic technique allowed surgeons to directly observe the structure inside a tumor cavity in high-definition. In the present study, 24 patients had pituitary macroadenomas or microadenomas that did not invade the cavernous sinus, and were considered to have undergone successful total resection. Among these patients, no tumor residues were observed through the diving endoscopic technique. Some white lichenoid or fibrous cord-like tissues in the tumor cavity were considered to be remnants of tumors. However, pathology confirmed that these were not tumor tissues. For tumors that invaded the cavernous sinus in 13 patients, observation could only be conducted under the angulation endoscope of the diving endoscope; i.e., the operation could not be conducted under an endoscope. The present study suggests that the diving endoscopic technique may be used to directly observe the resection extent of tumors within the tumor cavity, especially the structure of the tumor cavity inside the sella turcica. The present study also directly validates the reliability of pituitary adenoma resection under endoscope-assisted microscope. In addition, the diving endoscopic technique also allows the surgeon to observe the underwater environment within the sella turcica.

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Introduction

At present, intraoperative computed tomography and magnetic resonance imaging (MRI) examination results are used as objective evidence for evaluating the presence of a residual tumor during pituitary adenoma resection surgery via the trans-nasal-sphenoidal approach, especially for the pituitary macroadenomas that have invaded the upper sella turcica or cavernous sinus. These examinations improve tumor resection and cure rates. However, intraoperative MRI images may be influenced by blood clots, collapsed tumor cavities and hemostatic materials; which affects the evaluation of residual tumors, especially for small residual tumors within the sella turcica. In addition, special surgical instruments and an operating room are needed for intraoperative MRI, which is expensive; therefore, this is not commonly conducted (1-9). Following trans-nasal-sphenoidal pituitary tumor resection, it may not be possible to observe the internal structure of the tumor cavity under microscopy and conventional endoscopy due to the depression of the diaphragma sellae or bleeding from the tumor cavity; therefore it may not be clearly and accurately evaluated whether residual tumors are present in the tumor cavity (9).

In the last decade, the application of routine endoscopic techniques in surgery for pituitary adenoma has been rapidly developed due to its characteristics of close lighting, wide field of vision and production of high quality images, as well as improved outcomes and fewer complications; traits which have been recognized by many neurosurgeons (10-18). The extended transsphenoidal endoscopic technique has certain advantages in processing lesions in the midline of the skull base such as clival chordoma, cystic craniopharyngioma and tuberculum sellae meningiomas (19-23). It has previously been reported that the use of endoscopic techniques in the treatment of lesions in the region of the lateral skull base such as Meckel's cavity and the petroclival region also achieved satisfactory results (24-27). An endoscope is often used to accommodate for the blind spots of the microscope, and a microscope may also make up for shortcomings of the endoscope, such as the two-dimensional image, image deformation and the space occupied by the endoscope itself. The application of the diving endoscopic technique in surgery for pituitary adenoma has been reported previously (28,29). This makes up for the shortcomings of the microscope and conventional endoscope, in which, due to tumor cavity bleeding or hemorrhage of the cavernous sinus, microstructures in the tumor cavity may not be clearly observed under microscopy or conventional endoscopy. This combined technique may directly determine the presence of residual tumors in the tumor cavity, providing an objective basis in evaluating the resection extent of pituitary adenoma. In the present study, the diving endoscopic technique has been applied in 37 patients who underwent pituitary adenoma resection surgery via the trans-nasal-sphenoidal approach, which is reported below.

Materials and methods

Clinical data. From October 2011 to July 2014, a total of 37 patients (17 male, 20 female; age range 28-70 years) with pituitary adenoma from the Department of Neurosurgery in Beijing Boai Hospital (Beijing, China) were treated by applying the diving endoscopic technique. The inclusion criteria for using trans-nasal-sphenoidal approach were as follows: i) Tumors that had developed above the suprasellar level did not exceed the level of the interventricular foramen; ii) tumors that had developed above the suprasellar level did not exceed 2 cm in midline; and iii) the advancing tumor did not exceed the tuberculum sellae level.

Among these 37 patients, according to the pre-opration pituitary related hormone levels, 15 patients exhibited prolactin-secreting adenoma, 14 patients exhibited nonfunctioning pituitary adenoma, 3 patients exhibited adrenocorticotropic hormone-secreting adenoma, and 5 patients exhibited growth hormone (GH)-secreting adenoma. Among the 5 patients with GH type, 4 patients had recurrent pituitary adenoma, whereas 1 patient exhibited pituitary adenoma apoplexy. Furthermore, among the 37 patients with pituitary adenoma, 3 patients had micro pituitary adenoma, 29 patients had large pituitary adenoma, and 5 patients had giant pituitary adenoma. Furthermore, 5 patients underwent tumor resection via the extended trans-nasal-sphenoidal approach.

The clinical symptoms exhibited by patients are as follows: Simple headache (n=2), simple amenorrhoea and lactation (n=2), simple decreased visual acuity (n=12), simple acromegalic face change (n=3), headache with decreased visual acuity (n=4), headache with acromegalic face changes (n=1), headache and eye movement disorder with decreased visual acuity (n=1), decreased visual acuity with amenorrhea and lactation (n=4), decreased visual acuity with acromegaly (n=1), progressive obesity and elevated blood pressure (n=2), obesity and breast development (n=1), asymptomatic (n=1) and sexual function decline (n=3) The present study was approved by the Beijing Boai Hospital, China Rehabilitation Research Centre. Written informed consent was provided by all patients.

Surgical methods. Initially, a unilateral trans-nasal-sphenoidal approach was set under a surgical microscope, and tumor resection was conducted under microscope or endoscope. The structure in the tumor cavity was observed by applying the diving endoscopic technique following confirmation of complete resection of the tumor.

This approach was typically set at the left side of the nasal cavity, however, if the tumor is clearly at the left side, the right side was selected. For tumors that had obviously invaded the cavernous sinus, extended trans-nasal-sphenoidal approach for tumor resection was set at the ipsilateral nasal cavity, and part of the middle turbinate was removed for lateral expansion. The patient was placed in the supine position, the surgeon stood at the right side of the patient, the patient's body was situated close to one side of the surgeon and the head was slightly turned to the right. The scopes of the lateral wall of the sphenoidal sinus, the bone and dura of the sellar base, and the cavernous sinus, which were to be opened, were determined according to the size and location of the tumor; thus, resection surgery was conducted under microscopy or endoscopy. When the effect of the resection under endoscope-assisted microscopy was satisfactory, observation was conducted by applying the diving endoscopic technique.

A KARL STORZ LOTTA high-definition endoscope (KARL STORZ GmbH & Co. KG., Tuttlingen, Germany) was used. Images were acquired by applying a hard observing endoscope of 0 and 30˚, with a diameter of 2.7 mm and a length of 18 cm. The flow-operating sheath was externally connected with a 500-ml sterile saline infusion bag. An infusion pressure bag was used to provide pressure, which was set at 100 mmHg, in order to provide a relatively large injection speed and injection pressure. If the flow-operating sheath was not connected with any suction device, turbulence would occur and affect the definition of the visual field. The attractor was directly placed in the nasopharynx to prevent any disruptions on the imaging effect provided by the diving endoscopic technique. A cavity was formed following tumor resection, the endoscope was placed in the tumor cavity, and the saline bag was pressurized to rapidly fill-up the tumor cavity; thus, enabling the visual field to clear. Due to the difference in refractive index between water and air, reducing the focal length was required at this point.

Patients were followed up for 3 months, and assessed for visual acuity, transient diabetes insipidus, hypopituitarism, cerebrospinal fluid leakage and tumor recurrence.

Histopathology. Following resection, *s*uspected tumor specimens were fixed with 4% formalin at room temperature for ≥6 h. Specimens were subsequently cut into 3 μm sections and stained with hematoxylin for 10 min at room temperature, and eosin for 3 min at room temperature. Samples were then viewed under light microscopy at x40 and x100 magnification.

Results and Discussion

The diving endoscopic technique allows surgeons to directly observe the structure inside the tumor cavity in high-definition. In the present study, 24 patients had pituitary macroadenomas or microadenomas that did not invade the cavernous sinus, and were considered to have undergone successful total resection; and no tumor residues were observed through the diving endoscopic technique in any of these patients. It was initially considered that some of the white lichenoid and fibrous cord-like tissues in the tumor cavity were remnants of tumors. However, pathology confirmed that this was not the case. For tumors that invaded the cavernous sinus, which occurred in 13 patients, observation was only able to be conducted under an angulation endoscope through the diving endoscopic technique; i.e., surgery could not be conducted under an endoscope.

Of the total 37 patients, 1 developed cerebrospinal leakage following surgery, which was ameliorated via lumbar cistern drainage for 5 days. No patients developed intracranial infection. Furthermore, among these patients, 1 had visual acuity of hand-motion prior to surgery, which did not improve following surgery; whereas short-term symptoms, such as headache and impaired vision, were improved in other patients. The mean duration of surgery was ~1.5 h, which was approximately twice as long than by a microscope alone. In the present study, it was found that the application of the diving endoscopic technique did not increase the incidence of postoperative cerebrospinal leakage and intracranial infection.

The application of the diving endoscopic technique in surgery for pituitary adenoma has increased the exposure of the surgical field. In particular, the application of an angulation endoscope is able to increase the exposure of the lateral line (Fig. 1), However, due to continuous bleeding of the tumor cavity or hemorrhage of the cavernous sinus, the observation of the local structure of tumor cavity through conventional endoscopic techniques could not be conducted. Although there was no active bleeding in the tumor cavity, due to the reflection effect of blood clots that cover the wound surface and liquid on the structure surface, the visual field was not clear. In addition, it was impossible to clearly determine the presence of residual tumors under direct vision as the sinking diaphragma sellae was blocked following tumor resection. Senior *et al* (29) reported the application of the diving endoscopic technique in pituitary adenomas in 2005. This technique allows the endoscope to more clearly present local subtle structures in tumor cavities.

At present, the objective basis is to determine the degree of pituitary adenoma resection, which is primarily obtained through intraoperative MRI. MRI is beneficial, particularly in the evaluation of residual tumors in the lateral side of the internal carotid artery within the cavernous sinus, as hemorrhage, collapse of the tumor cavity and the application of hemostatic material may affect MRI imaging, which may affect the evaluation of residual tumors in the sella turcica (1,2,5,8). The application of the diving endoscopic technique may allow the surgeon to directly observe the structure in the tumor cavity, and clearly determine the presence of residual tumors in the sella turcica under direct view. In the present study, following the surgical resection of tumors under a microscope or endoscope, some white lichenoid or fibrous cord-like structures were observed in the medial wall of the cavernous sinus, diaphragma sellae fold returns and suprasellar tissues in some patients (n=6; Fig. 2), through the application of the diving endoscopic technique. Initially, these were considered to be remnants of tumors, and were resected with a straight or elbow bipolar elctrocoagulation forcep (Fig. 3). Histopathological examination of these specimens was performed, and confirmed that these were not tumor tissues, but were venous sinus-like structures formed by small amounts of pituitary tissues and dense fibrous connective tissues (Fig. 4).

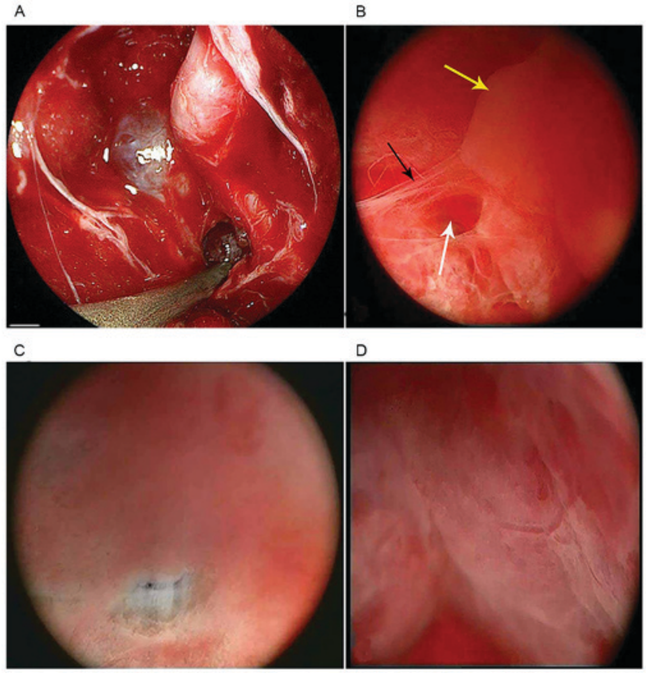

Figure 1. (A) Endoscopic resection of cavernous sinus tumors reveals the internal carotid artery in the cavernous sinus. (B) The tumor is turned from the medial wall of the cavernous sinus (yellow arrow), revealing the defective part of the medial wall of the cavernous sinus (white arrow); and a fibrous cord lies between the tumor and the medial wall of the cavernous sinus (black arrow). (C) Small leaks in the diaphragma sellae have been probed. (D) Following resection of soft texture tumors, it was observed that the medial wall of the cavernous sinus was smooth.

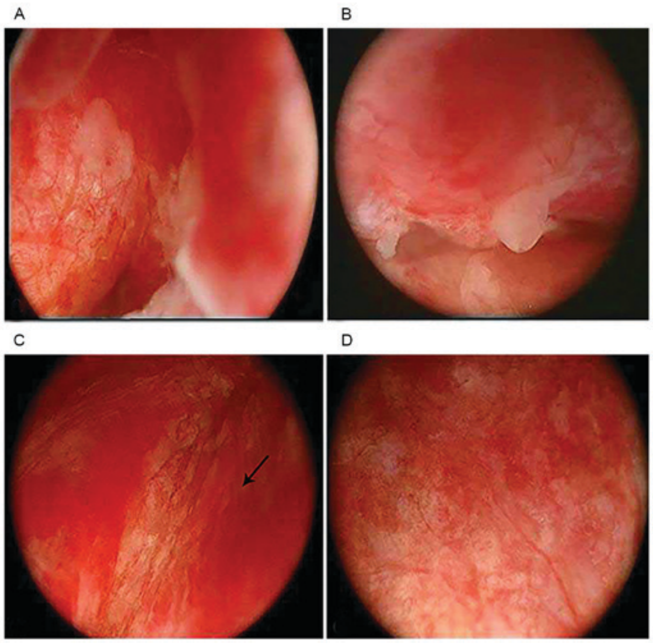

Figure 2. Fold return structures in the diaphragma sellae are shown following tumor resection. (A and B) Fibrous cord-like structures in fold returns of the diaphragma sellae are shown. (C) Remnants of white lichenoid tissues in the fold returns of the diaphragma sellae and the medial wall of the cavernous sinus (black arrow). (D) Remnants of white lichenoid tissues in the diaphragma sellae.

It is possible to determine the extent of tumor resection under direct vision by applying the diving endoscopic

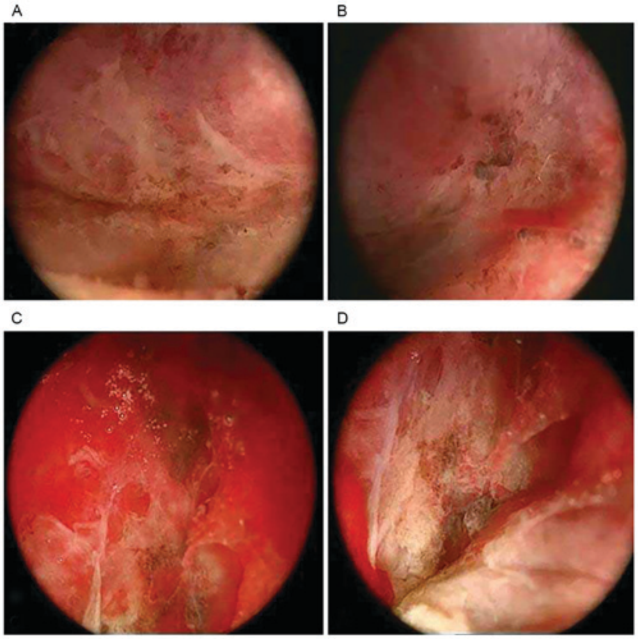

Figure 3. Removal of suspected residual tumors in the fold returns of the (A and B) diaphragma sellae, (C) the inside wall of the cavernous sinus, and (D) the diaphragma sellae by bipolar electric coagulation.

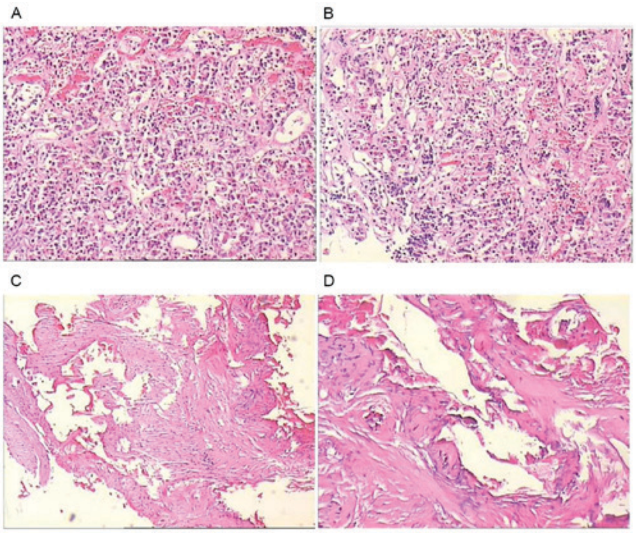

Figure 4. (A and B) Acinar structures formed by mixed pituitary cells are rich in sinusoidal vessels among the acini, as indicated by hematoxylin and eosin staining (A, low magnification, x40; B, moderate magnification, x100). (C and D) Venous sinus-like structures formed by dense fibrous tissues (C, low magnification, x40; D, moderate magnification, x100).

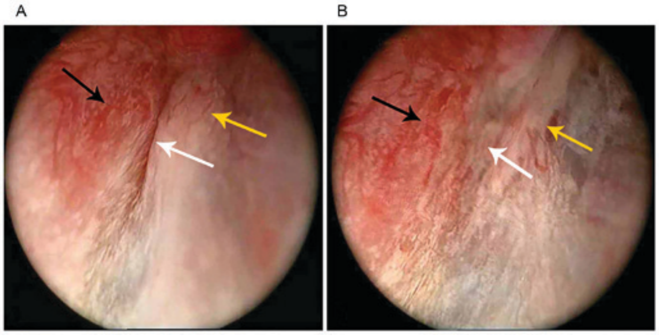

Figure 5. (A) A fold return (white arrow) was formed between the medial wall of the cavernous sinus (black arrow) and the diaphragma sellae (yellow arrow). (B) The diaphragma sellae (yellow arrow) is gradually elevated with increased injection pressure, showing the white lichenoid tissues in the fold returns (white arrow).

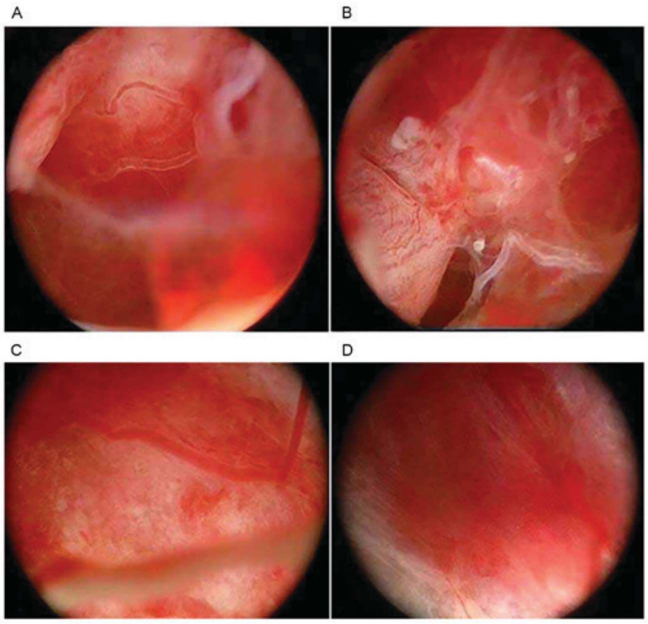

Figure 6. (A and B) Bleeding points in the suprasellar arachnoid perforator artery and arachnoid. (C) Bleeding points in the diaphragma sellae. (D) Bleeding points in the medial wall of the cavernous sinus.

technique. In addition, this study has identified the following advantages: i) It is known that the collapse of the diaphragma sellae into the sella is one of the important factors that influence tumor resection, and tumor residues often occur in fold returns of the diaphragma sellae (16). By using changes in water pressure, the diving endoscopic technique is able to elevate the diaphragma sellae, in order to observe whether residual tumors in the fold returns of the diaphragma sellae are present, especially the fold returns between the diaphragma sellae and medial wall of the cavernous sinus (Fig. 5). ii) The pressure of the water injection also has an effect in controlling bleeding. iii) In reparatory surgery of cerebrospinal leakage, the endoscope may be used to search for leaks (Fig. 1C). Furthermore, the endoscope may also be used to explore bleeding points, particularly in the sella turcica. During the resection of tumors located in the sella turcica, it is possible to cause intracranial hemorrhage due to damage to the suprasellar blood vessels. Surgeons are able to search bleeding points along the surgical channel and decide whether active measures should be taken (Fig. 6).

In the present study, the following disadvantages of the diving endoscopic technique were observed. i) Local microscopic anatomy is complex, and the surgery must be conducted by surgeons who are familiar to the anatomical structures in the sellar region. ii) Imaging lacks stereo feeling. When tumors were removed under the endoscope, they were relatively close to the endoscope, which led to the difficult operation of the scraper ring and elbow bipolar electric coagulation under the microscope.

Furthermore, it has been realized through this study that the following surgical conditions are required for the application of the diving endoscopic technique. i) First, a tumor cavity ≥1 cm^2 is needed, in which an endoscope may be placed and the tumor cavity to be observed may be filled up with physiological saline in a short time. ii) The maintenance of a clear field of vision requires the rapid replacement of normal saline for lavage in tumor cavity. The tumor cavity may be rapidly filled with saline thus quickly replacing cerebrospinal fluid. iii) Rapid bleeding in the tumor cavity must be prevented; that is, the replacement of blood-water in the tumor cavity must be faster than the bleeding.

Endoscopic techniques have increased the present understanding of the surgery of pituitary adenomas, and have also lead to some questions. It was detected that during tumor resection, parts of the medial wall of the cavernous sinus and pituitary around the tumors were smooth in some patients (Fig. 1D). In addition, the medial wall of the cavernous sinus around the tumor was rough, uneven, and even presented with defects in some patients (Fig. 1B). Further studies are required to determine whether this is associated with tumor invasion.

In conclusion, the diving endoscopic technique enables the further understanding of the intrasellar local subtle anatomy *in vivo*, allows the direct and clear view of the intrasellar structure and provides more convenient, economical, objective evidences for determining the resection extent of intrasellar tumors during the operation.

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