Individualized surgical strategies for Rathke cleft cyst based on cyst location

Clinical article

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Object. An assessment regarding both surgical approaches and the extent of resection for Rathke cleft cysts (RCCs) based on their locations has not been reported. The aim of this study was to report the results of a large series of surgically treated patients with RCCs and to evaluate the feasibility of individualized surgical strategies for different RCCs.

Methods. We retrospectively reviewed 87 cases involving patients with RCCs (16 intrasellar, 50 intra- and suprasellar, and 21 purely suprasellar lesions). Forty-nine patients were treated via a transsphenoidal (TS) approach, and 38 were treated via a transcranial (TC) approach (traditional craniotomy in 21 cases and supraorbital keyhole craniotomy in 17). The extent of resection was classified as gross-total resection (GTR) or subtotal resection (STR) of the cyst wall. Patients were thus divided into 3 groups according to the approach selected and the extent of resection: TS/STR (n = 49), TC/STR (n = 23), and TC/GTR (n = 15).

Results. Preoperative headaches, visual dysfunction, hypopituitarism, and diabetes insipidus (DI) resolved in 85%, 95%, 55%, and 65% of patients, respectively. These rates did not differ significantly among the 3 groups. Overall, complications occurred in 8% of patients in TS/STR group, 9% in TC/STR group, and 47% in TC/GTR group, respectively (p = 0.002). Cerebrospinal fluid (CSF) leakage (3%), new hypopituitarism (9%), and DI (6%) were observed after surgery. All CSF leaks occurred in the endonasal group, while the TC/GTR group showed a higher rate of postoperative hypopituitarism (p = 0.7 and p < 0.001, respectively). It should be particularly noted that preoperative hypopituitarism and DI returned to normal, respectively, in 100% and 83% of patients who underwent supraorbital surgery, and with the exception of 1 patient who had transient postoperative DI, there were no complications in patients treated with supraorbital surgery. Kaplan-Meier 3-year recurrence-free rates were 84%, 87%, and 86% in the TS/STR, TC/STR, and TC/GTR groups, respectively (p = 0.9).

Conclusions. It is reasonable to adopt individualized surgical strategies for RCCs based on cyst location. Gross-total resection does not appear to reduce the recurrence rate but increase the risk of postoperative complications. The endonasal approach seems more appropriate for primarily intrasellar RCCs, while the craniotomy is recommended for purely or mainly suprasellar cysts. The supraorbital route appears to be preferred over traditional craniotomy for its minimal invasiveness and favorable outcomes. The endoscopic technique is helpful for either endonasal or supraorbital surgery.

(http://thejns.org/doi/abs/10.3171/2013.8.JNS13777)

Key Words • endoscopy • pituitary surgery • Rathke cleft cyst • supraorbital craniotomy • transsphenoidal surgery

Rathke cleft cysts (RCCs) are regarded as benign cystic lesions derived from a remnant of the Rathke pouch. They are common findings at autopsy, with a reported incidence of 5% to 33%, and account for 6%–10% of sellar lesions.3,9,17,32,39,46 Although mostly asymptomatic, some RCCs can become sufficiently large to cause compressive effect on surrounding structures, resulting in neurological and endocrine disturbances. As a result, surgical intervention is recommended for symptomatic or at-risk patients.

Traditionally, the 2 most common surgical approaches are the endonasal transsphenoidal route and the standard craniotomy. The endonasal approach is typically used for sellar lesions, whereas the craniotomy is indicated for suprasellar lesions.2,11,38,40 Owing to its reduced invasiveness...
and satisfactory outcomes, the endonasal approach has been preferred over standard craniotomy in 85% to 100% of the patients in recent years. Even in the setting of RCCs with suprasellar location, multiple cases of extended transsphenoidal approaches for cyst removal have also been reported. Other minimally invasive approaches, such as the supraorbital keyhole craniotomy, although being increasingly used to access sellar or parasellar tumors, have not yet been employed in removing RCCs.

As we know, the relationship between the RCC and the normal pituitary gland varies among individuals. Thus, if gland injury is to be avoided, a single surgical approach cannot be optimal for all patients. An assessment of the relative benefits and potential pitfalls of different approaches based on cyst location is required in order to individualize surgical strategies for RCC. However, few authors have characterized the anatomical location of RCCs in their studies, and the evaluation of different approaches based on cyst location has not previously been reported. In addition, the extent of resection of cyst wall remains somewhat controversial. For these reasons, we present a large series of cases involving patients who underwent surgery for RCC over a 10-year period. We describe our experience with different approaches and compare their surgical outcomes. Our main purpose in undertaking this work was to provide some recommendations regarding the individualized surgical treatment of a given patient with RCC.

**Methods**

**Patient Population**

Between 2002 and 2012, 87 patients with RCCs were surgically treated at Nanfang Hospital, Southern Medical University, Guangzhou, China. The indications for surgery included specific symptoms associated with cysts, laboratory evidence of hypopituitarism, documented lesion growth, or uncertain diagnosis. Pathological diagnosis was confirmed by identifying non-neoplastic epithelial cells and/or the presence of amorphous material. Each patient’s history, presenting symptoms, endocrine status, operative procedure, imaging findings, pathology reports, and clinical outcomes were retrospectively reviewed. A detailed neurological history was obtained in all cases, and all patients underwent physical examinations, pituitary function tests, 3D CT scans, and MRI before and after surgery.

**Preoperative Evaluation**

Preoperative pituitary function was evaluated by checking levels of adrenocorticotropic hormone, growth hormone, insulin-like growth factor, prolactin, thyroid-stimulating hormone, thyroxin, follicle-stimulating hormone, luteinizing hormone, and testosterone as well as the morning cortisol level. Cyst characteristics, including cyst size, imaging presentation, and cyst location, were documented in all cases on preoperative imaging. The cyst size was determined by the maximum diameter on sagittal or coronal MRI. Of the total population, 16 patients (18%) had an entirely intrasellar RCC (Fig. 1A and B), 21 (24%) had a purely suprasellar lesion (Fig. 2A and B), and 50 (58%) had a sellar lesion with suprasellar extension (Fig. 3A and B) (Table 1).

**Surgical Techniques**

Two surgical approaches were used for removal of RCCs: transsphenoidal (TS, n = 49) and transcranial (TC, n = 38). The selection of approach was based on cyst location on preoperative MRI. The essential principle is to avoid manipulating the normal pituitary gland in the path of the surgical route, and to minimize the risk of gland injury. We used the transsphenoidal approach to remove intrasellar RCCs (n = 16) or intra- and suprasellar RCCs with only thin portion or absence of gland occupying the sellar floor (n = 33) (Table 1). In contrast, the transcranial route was employed to access purely suprasellar cysts (n = 21), intra- and suprasellar cysts with gland covering a major part or most of the sellar floor (n = 17). Between 2002 and 2006, traditional craniotomies were performed in 18 cases. Since 2006, a supraorbital keyhole approach was employed for 17 cases; traditional craniotomies were only used for 3 lesions of uncertain diagnosis. The extent of resection was classified as gross-total resection (GTR) or subtotal resection (STR) of the cyst wall based on video recording of the surgical procedure and postoperative imaging. Patients were thereby divided into 3 groups according to the approach selected and the extent of resection: TS/STR (n = 49), TC/STR (n = 23), and TC/GTR (n = 15).

**Endoscopic Endonasal Transseptal Transsphenoidal Approach**

An endonasal transseptal technique was used to access the sphenoid sinus. To minimize damage to the pituitary gland, the dural incision was determined by the location of the residual gland, as identified on preoperative imaging. Typically, the opening was positioned over the cyst floor or the thinnest portion of the residual gland (Fig. 1E). The maximum diameter of the cyst opening was 4–6 mm, depending on cyst size. All cyst contents were completely removed without gland manipulation, and the cyst wall that did not adhere to the pituitary gland was partially resected. The whole procedure was performed under an endoscope, providing better visualization of the inner cyst. At the completion of cyst removal, if there was no defect in the suprasellar arachnoid, hydrogen peroxide was placed in the cyst cavity for about 2 minutes. The sellar floor was left open in cases without CSF leak, allowing for marsupialization of cysts into the sphenoid sinus (Fig. 1F). If CSF leakage with a dural or arachnoid tear of more than 2 mm was found during the operation, sellar floor reconstruction was performed with autologous fat packing. Smaller CSF leaks (tear length ≤ 2 mm) were typically repaired using multilayer patches of collagen sponge without packing. Lumbar drain was not routinely placed after surgery.

**Traditional Craniotomy**

As mentioned above, traditional craniotomy was the
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only transcranial approach used prior to 2006. Similar to surgery for other lesions of the sellar region, RCC surgery was typically performed via a subfrontal or pterional approach, which has been described elsewhere.2,16,38 The surgical purpose was to evacuate the cyst contents completely and excise the cyst wall whenever possible. The site of the cyst incision was determined by the location of the pituitary gland, as revealed on preoperative imaging. Radical resection of the cyst wall was performed in our early 15 cases with the intention of reducing the recurrence rate.

Supraorbital Keyhole Cranietomy

The skin incision was placed within the eyebrow, extending from the supraorbital notch to the brow’s lateral limit. Special care should be taken at the medial aspect of the incision to avoid injury to the supraorbital nerve. A craniotomy was then performed, measuring approximately 15–20 mm × 20–25 mm. After the dural incision, the sylvian cistern was opened and CSF was drained to promote brain relaxation. The RCC and its adjacent structures, including the optic chiasm, optic nerves, internal carotid arteries, and infundibulum, were identified (Figs. 2E and 3E). All cyst contents were totally removed, and the cyst wall was partially resected without transgressing surrounding structures (Fig. 3F). Finally, the cyst was left open, allowing for its drainage into the suprasellar cistern (Figs. 2F and 3G). The dura was then closed in a watertight fashion, and the bone flap was repositioned.

Fig. 1. A case of an intrasellar RCC treated by an endoscopic endonasal route. A and B: Preoperative T1-weighted Gd-enhanced sagittal and coronal MR images demonstrating a 13-mm cyst with an entirely intrasellar location. The sagittal image (A) shows the cyst arising between the anterior and posterior lobes, with only a small amount of residual gland left overlying the sellar floor (arrow). Therefore, an endonasal approach, which may minimize damage to the gland, was suitable for this case. C and D: Postoperative T1-weighted Gd-enhanced sagittal and coronal MR images demonstrating resection of the cyst. E and F: Intraoperative endoscopic photographs showing incision and evacuation of the cyst (E) and the cyst floor left open after resection (F), with the residual gland remaining intact. CC = cyst contents; DS = diaphragma sellae; PG = pituitary gland.

Fig. 2. A case of a suprasellar RCC treated by a fully endoscopic supraorbital route. A and B: Preoperative T1-weighted Gd-enhanced sagittal and coronal MR images demonstrating a 15-mm cyst with purely suprasellar location. The sagittal image (A) shows the normal gland (arrow) occupying the entire sellar space, and an endonasal approach could therefore cause a higher risk of gland injury. C and D: Postoperative T1-weighted Gd-enhanced sagittal and coronal MR images demonstrating resection of the cyst. E and F: Intraoperative endoscopic photographs showing identification of the cyst and its adjacent structures (E) and partial removal of the cyst wall (F), performed without damage to the pituitary gland and the infundibulum. The cyst was left open, allowing for its drainage into the suprasellar cistern. ICA = internal carotid artery; OC = optic chiasm; PS = pituitary stalk; RCC = Rathke cleft cyst; TS = tuberculum sellae.
and fixed. The skin was closed with a running absorbable intradermal suture. Early in our experience, as reported by most other authors, the supraorbital approach was performed with an operating microscope, sometimes assisted by an endoscope. In recent years, however, we developed a purely endoscopic technique through an eyebrow supraorbital route, which combines an enhanced visualization and the absence of brain retraction. This technique was successfully used in the last 8 patients of our series (Figs. 2 and 3).

Postoperative Evaluation

Postoperative surgical outcomes were recorded in each case, including symptom improvement, endocrine assessment, complications, and recurrences. An immediate postoperative MRI study was obtained within 48 hours of surgery to evaluate the extent of removal. Routine follow-up MRI studies were scheduled at 3 and 9 months postoperatively and then annually thereafter. Pituitary function was monitored by hormone level assessment at 1, 3, 6, and 12 months after surgery. Radiological recurrence was defined as reaccumulation of cyst contents demonstrated on follow-up imaging compared with the immediate postoperative MRI. Symptomatic recurrence was defined by repeated surgery for symptoms related to the reaccumulation.

Statistical Analysis

We used a Student t-test or analysis of variance to compare continuous variables (age, cyst diameter, and follow-up period). Independent categorical variables (sex, cyst location, preoperative presenting symptoms, postoperative symptom improvement, complications, and recurrence) were compared by use of the chi-square test.

| TABLE 1: Distribution of cases according to cyst location and surgical approach* |
|-----------------|----------------|----------------|----------------|
|                  |                 | Transsphenoidal (n = 49) | Transcranial |
|                  |                 |                             | Traditional (n = 21) | Supraorbital (n = 17) |
| Cyst Location    | Total (n = 87)  |                             |                   |                     |
| intrasellar      | 16 (18%)        | 16 (33%)                    | 0 (0%)            | 0 (0%)              |
| intra- & suprasellar | 50 (58%)      | 33 (67%)                    | 10 (48%)          | 7 (41%)             |
| suprasellar      | 21 (24%)        | 0 (0%)                      | 11 (52%)          | 10 (59%)            |

* Values represent numbers of cases (%).
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or Fisher exact test. When assessing improvement in any given symptom, only those patients presenting with that symptom were included. Kaplan-Meier analysis was used to assess radiological recurrence rates among different surgical groups. All statistical analyses were performed using SPSS software (Version 19.0; SPSS Inc.). The data were expressed as means ± standard deviation. A p value of 0.05 was considered as statistically significant, and all tests were 2-tailed.

**Results**

**Patient Demographic Data**

Table 2 shows the population demographic data for the overall cohort and each group. The overall average age of the patients was 41 ± 14 years (range 10–73 years), and 64 (74%) of the 87 patients were female. There was no significant between-groups difference with respect to age or sex. The maximum cyst diameter on preoperative MR images averaged 14 mm, 17 mm, and 18 mm in the TS/STR, TC/STR and TC/GTR groups, respectively (p = 0.1). The overall mean duration of follow-up was 46 ± 29 months (range 3–122 months); there was no statistically significant between-groups difference (p = 0.3).

**Preoperative Presentations**

Headache was the most frequent initial symptom, occurring in 66 cases (76%). Visual disturbance was reported in 39 (45%) patients. Preoperative hyperprolactinemia, hypopituitarism, and DI were found in 31 (36%), 29 (33%), and 17 (20%) of the patients, respectively. Thirty-one patients had more than one of these presenting symptoms. The incidence of headache, visual dysfunction, and hyperprolactinemia did not vary significantly between the groups. However, the patients in the TS/STR group had a higher incidence of hypopituitarism than those in the TC/GTR group (p = 0.001). In contrast, there was a trend toward a more common DI in either TC group compared with TS group (p = 0.001). In the 29 patients with hypopituitarism, hypocortisolism was the most common dysfunction (24%), followed by hypothyroidism (20%), hypogonadism (15%), and growth hormone deficiency (10%) (Table 3). Fourteen patients had hormonal deficiency in 2 or more hormonal axes.

**Surgical Outcomes**

The cyst contents were completely removed in all cases. Surgical repair was performed in 11 of 49 patients who were treated by endonasal route due to intraoperative CSF leak. Preoperative headaches improved in 56 (85%) of 66 patients (Table 4). Of the 39 patients presenting with visual dysfunction, 37 (95%) experienced an improvement following surgery. Hyperprolactinemia improved remarkably in 29 (94%) of 31 patients. In contrast, hypopituitarism resolved in only 16 (55%) of 29 patients, and DI in 11 (65%) of 17 patients. The percentages of patients with improved outcome did not differ significantly between groups. However, it should be noted that hypopituitarism and DI, respectively, resolved in 100% and 83% of patients who underwent supraorbital keyhole surgery. Specific hormonal axes of hypopituitarism that improved after surgery are shown in Table 3. Recovery was observed in 62% of patients with hypocortisolism and 54% of patients with hypogonadism, while growth hormone deficiency and hypothyroidism resolved in only 33% and 35% of patients, respectively.

**Complications**

Complications resulting from surgery included CSF leak, new-onset hypopituitarism, and DI. No other events

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**TABLE 2: Population demographic data**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total (n = 87)</th>
<th>Group</th>
<th>p Value</th>
<th>Group</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>TS/STR (n = 49)</td>
<td>TC/STR (n = 23)</td>
<td>TC/GTR (n = 15)</td>
<td>Overall</td>
</tr>
<tr>
<td>age (yrs)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>mean</td>
<td>41 ± 14</td>
<td>40 ± 12</td>
<td>42 ± 17</td>
<td>42 ± 14</td>
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<td>10–69</td>
<td>19–73</td>
<td>20–65</td>
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<tr>
<td>female</td>
<td>64 (74%)</td>
<td>36 (73%)</td>
<td>16 (70%)</td>
<td>12 (80%)</td>
<td>0.8</td>
</tr>
<tr>
<td>mean max cyst diameter (mm)</td>
<td>16 ± 7</td>
<td>14 ± 5</td>
<td>17 ± 6</td>
<td>18 ± 7</td>
<td>0.1</td>
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<tr>
<td>follow-up (mos)</td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mean</td>
<td>46 ± 29</td>
<td>48 ± 27</td>
<td>39 ± 31</td>
<td>52 ± 33</td>
<td>0.3</td>
</tr>
<tr>
<td>range</td>
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<td>6–122</td>
<td>3–94</td>
<td>3–108</td>
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<td>presentation</td>
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<tr>
<td>headache</td>
<td>66 (76%)</td>
<td>40 (82%)</td>
<td>15 (65%)</td>
<td>11 (73%)</td>
<td>0.3</td>
</tr>
<tr>
<td>visual dysfunction</td>
<td>39 (45%)</td>
<td>19 (39%)</td>
<td>11 (48%)</td>
<td>9 (60%)</td>
<td>0.3</td>
</tr>
<tr>
<td>hyperprolactinemia</td>
<td>31 (36%)</td>
<td>14 (29%)</td>
<td>9 (39%)</td>
<td>8 (53%)</td>
<td>0.2</td>
</tr>
<tr>
<td>hypopituitarism</td>
<td>29 (33%)</td>
<td>24 (49%)</td>
<td>2 (9%)</td>
<td>3 (20%)</td>
<td>0.001</td>
</tr>
<tr>
<td>DI</td>
<td>17 (20%)</td>
<td>3 (6%)</td>
<td>8 (35%)</td>
<td>6 (40%)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

* Values represent numbers of patients (%) unless otherwise indicated. GTR = gross-total resection; STR = subtotal resection; TC = transcranial; TS = transsphenoidal.
such as visual worsening, meningitis or hemorrhage were documented in our series. As described in Table 4, overall complications occurred in 4 (8%) of the patients in the TS/STR group, 2 (9%) of the patients in TC/STR group, and 7 (47%) of the patients in TC/GTR group (p = 0.002). Postoperative CSF leak was present in 3 patients, all of whom had undergone endonasal surgery, although the finding was not statistically significant (p = 0.7). Through bedrest and/or lumbar drainage, the CSF leakage resolved in all patients without further surgical repair. Postoperatively, patients in the TC/GTR group had a significantly higher incidence of new anterior pituitary deficiency than those in either the TS/STR or the TC/STR group (p < 0.001). Five patients (6%) experienced new DI, whether temporary or permanent; no significant difference was found among the 3 groups (p = 0.1). Permanent DI occurred in only 1 patient (who underwent radical craniotomy). In the 17 patients who underwent supraorbital craniotomy, the only documented postoperative complication was 1 case of transient DI.

Recurrence

During the follow-up period, radiological recurrence was observed in 7 (14%) of 49 patients in the TS/STR group, 2 (9%) of 23 in the TC/STR group, and 2 (13%) of 15 in the TC/GTR group (p = 0.9). The mean time to recurrence for all patients was 14 ± 6 months (after the initial surgery). The Kaplan-Meier 3-year actuarial recurrence-free survival rate was 84% for the TS/STR group, 87% for the TC/STR group, and 86% for the TC/GTR group (Fig. 4). No significant difference was detected between groups (p = 0.9). Among the 7 patients with radiological recurrence who were treated via an endonasal approach, the recurrence rate appeared to be higher in patients who had undergone surgical repair of intraoperative CSF leak (4 [36%] of 11) than in patients who had not (3 [8%] of 38, p = 0.04). Finally, 7 of 11 patients with radiological evidence of recurrence required reoperation for symptomatic relapse. Two patients underwent a traditional craniotomy for cyst recurrence, and the other 5 patients underwent repeat endonasal surgery. No new deficits were noted in any patient who underwent resection of a recurrent cyst.

Discussion

Clinical Features

The overall demographic characteristics and clinical presentations of our patient group were in line with those of previously reported series of comparable size, and

### TABLE 3: Preoperative incidence of and postoperative improvement in specific hormonal axes of hypopituitarism*

<table>
<thead>
<tr>
<th>Hypopituitarism</th>
<th>Preop</th>
<th>Improved After Op</th>
</tr>
</thead>
<tbody>
<tr>
<td>overall</td>
<td>29 (33%)</td>
<td>16 (55%)</td>
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<tr>
<td>growth hormone deficiency</td>
<td>9 (10%)</td>
<td>3 (33%)</td>
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<tr>
<td>hypocortisolism</td>
<td>21 (24%)</td>
<td>13 (62%)</td>
</tr>
<tr>
<td>hypothyroidism</td>
<td>17 (20%)</td>
<td>6 (35%)</td>
</tr>
<tr>
<td>hypogonadism</td>
<td>13 (15%)</td>
<td>7 (54%)</td>
</tr>
</tbody>
</table>

* Values represent numbers of patients (%). The numbers in individual columns will not add up to the overall number because hormonal deficiency may occur in 2 or more hormonal axes.

### TABLE 4: Postoperative outcomes among different surgical groups*

<table>
<thead>
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<th>Parameter</th>
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</thead>
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<td></td>
<td></td>
<td>TS/STR (n = 49)</td>
<td>TC/STR (n = 23)</td>
</tr>
<tr>
<td>improved symptoms†</td>
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<td></td>
</tr>
<tr>
<td>headache</td>
<td>56 (85%)</td>
<td>36 (90%)</td>
<td>12 (80%)</td>
</tr>
<tr>
<td>visual dysfunction</td>
<td>37 (95%)</td>
<td>19 (100%)</td>
<td>10 (91%)</td>
</tr>
<tr>
<td>hyperprolactinemia</td>
<td>29 (94%)</td>
<td>14 (100%)</td>
<td>8 (89%)</td>
</tr>
<tr>
<td>hypopituitarism</td>
<td>16 (55%)</td>
<td>12 (50%)</td>
<td>2 (100%)</td>
</tr>
<tr>
<td>DI</td>
<td>11 (65%)</td>
<td>2 (67%)</td>
<td>6 (75%)</td>
</tr>
<tr>
<td>complications‡</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>overall</td>
<td>13 (15%)</td>
<td>4 (8%)</td>
<td>2 (9%)</td>
</tr>
<tr>
<td>postoperative CSF leak</td>
<td>3 (3%)</td>
<td>3 (6%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>new hypopituitarism</td>
<td>8 (9%)</td>
<td>2 (4%)</td>
<td>0 (0%)</td>
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<tr>
<td>new DI§</td>
<td>5 (6%)</td>
<td>1 (2%)</td>
<td>2 (9%)</td>
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<tr>
<td>recurrence</td>
<td></td>
<td></td>
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<tr>
<td>radiological</td>
<td>11 (13%)</td>
<td>7 (14%)</td>
<td>2 (9%)</td>
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<tr>
<td>symptomatic</td>
<td>7 (8%)</td>
<td>5 (10%)</td>
<td>1 (4%)</td>
</tr>
</tbody>
</table>

* Values represent numbers of patients (%) unless otherwise indicated.
† The percentage was calculated with respect to those patients presenting with preoperative symptoms.
‡ The numbers in individual columns will not add up to the total number of complications because more than one complication may occur in a single patient.
§ Permanent only in 1 patient, who was in the TC/GTR group.
there were no significant differences in age, sex distribution and cyst size among the 3 groups. There was also no significant between-groups difference in the incidence of preoperative headaches, visual dysfunction, or hyperprolactinemia, although we found a trend toward more common preoperative hypopituitarism in patients who underwent endonasal surgery. In contrast, patients treated by craniotomy had a higher incidence of DI. These findings are possibly related to our selection criteria for approach, which is determined by cyst location. In our series, we presented the largest collection of purely suprasellar RCCs to date (21 [24%] of 87 cases). Entirely intrasellar RCCs were all treated via an endonasal approach, whereas purely suprasellar RCCs were all treated via craniotomy. Suprasellar RCCs are thought to originate within the pars tuberalis, thus the infundibulum can be more easily involved, leading to DI.2,16,51 On the other hand, intrasellar RCCs with or without suprasellar extension, arising and developing in the sellar space, may exert more mass effect on the underlying adenohypophysis than suprasellar RCCs. As a result, the unequal distribution of cyst location between surgical groups may account for the differences of presentation.

Outcome Analysis

According to earlier reports,1,14,21,30,33,48 headache and visual problems are usually remarkably improved after surgery, whereas hypopituitarism and DI have a low likelihood of resolution. The low recovery rates are thought to be associated with an inflammatory process caused by the cyst contents, which may result in irreversible damage to the adjacent hypophysis.7,8,12,25,33,43,54 Our results show that preoperative headache and visual dysfunction were resolved in 85% and 95% of patients, and both rates compare favorably with the findings of other studies. However, we achieved better resolution in the patients with hypopituitarism and DI than other series of similar sample size (55% and 65%, respectively). This is probably due to our individualized surgical strategies based on cyst location. We chose a certain approach in consideration of avoiding transgression of the normal pituitary gland in the trajectory of the surgical route in order to minimize the risk of gland injury. Minimal manipulation of residual gland during the surgical procedure may also lead to a higher recovery rate.

The overall surgical complication rate in our series (15%) seems relatively high when compared with other reports.24,27,28,34,50 This is mainly because some patients underwent GTR. In analyzing the complications with respect to the extent of resection, 47% of patients with GTR had complications, whereas only 8% and 9% of those who underwent TS/STR and TC/STR had complications associated with surgery; this difference was significant (p = 0.002). In other words, 54% of complications (7 of 13) occurred in patients who underwent GTR. It should be noted that new hypopituitarism accounts for the majority of postoperative complications and contributes to the between-groups difference in overall complication rates. Moreover, of the 5 patients with new-onset DI, the only one in whom the condition was permanent was the one who had undergone GTR. All these results indicated that radical surgery may carry a greater risk of postoperative morbidity, as reported by other authors.1,13,24,34

Radiological recurrence occurred in 13% of the total population in our series over a median follow-up period of 46 months. This rate is consistent with prior studies. However, the range of recurrence rates in previous reports is quite large (0%–42%).1,8,11,13,15,23–25,28,34–36,47,53 Several factors, including sample size, surgical modalities, duration of follow-up, and definitions of recurrence, may account for the variation. For example, the radiological recurrence rate in our series was 13%, while the symptomatic recurrence rate was 8%. We also reported 3-year recurrence-free survival rates of 84%, 87%, and 86% in the TS/STR, TC/STR, and TC/GTR groups, respectively, with no significant between-groups difference—indicating a lack of additional benefit for GTR as compared with STR. This finding is in line with other reports. Aho et al.1 reviewed 118 cases of RCC, and concluded that there was no difference in recurrence rate between radical resection and decompression. Higgins et al.13 also found no significant advantage for GTR with respect to recurrence rate but did find that it was associated with more complications than less aggressive surgery. In addition, we found a possible association between a higher recurrence rate and graft packing for CSF leak, as some authors have mentioned.1,23,34 Nevertheless, more cases are needed for confirmation.

Assessment of Different Approaches

According to the literature,11,13,24,27,28,31,34–36,50 the trans-
The sphenoidal approach appears to be the mainstay of surgical treatment for RCCs because of its low morbidity and favorable outcomes. Some authors even attempted to remove RCCs with entirely suprasellar locations using an extended transsphenoidal approach. In contrast, a standard craniotomy is more invasive and usually requires retraction of cerebral lobes. It also remains unclear if a craniotomy can provide a better outcome for suprasellar RCCs than endonasal surgery. Moreover, some authors consider that the leakage of cyst contents within the suprasellar cistern may lead to the aseptic meningitis when using transcranial route. For these reasons, traditional craniotomy is only reserved for inaccessible suprasellar RCCs.

Although the transsphenoidal approach is considered an optimal surgical modality for RCCs, it still has several possible drawbacks. For purely suprasellar RCCs, or even some intrasellar RCCs with suprasellar extension, the residual normal gland is just located in the trajectory of the transsphenoidal route and usually requires an incision, which may increase the risk of postoperative hypopituitarism due to additional trauma to the already compromised gland (Figs. 2A and 3A). Similarly, to access the suprasellar lesions without transgressing the pituitary gland, a transstuberculum or transplanum approach may be used, thus the suprasellar cistern will be opened and a surgical repair will be required. Some authors have suggested, as shown in our results, that the overpacking of the cyst cavity for closure of CSF leak may increase the risk of recurrence. Furthermore, some authors even reported worsened vision after a transsphenoidal procedure due to the fat packing.

In recent years, the supraorbital keyhole craniotomy has been increasingly used to remove tumors of the sellar area. Numerous publications have demonstrated the advantages of this keyhole approach over traditional craniotomy, including minimal exposure, shortened surgical duration, lower morbidity, and satisfactory cosmetic outcomes. The significant strength of the supraorbital approach compared with the endonasal route is the lack of incision of the pituitary gland for purely or mainly suprasellar RCCs (Figs. 2F and 3H). This strength is further enhanced by endoscopic assistance, which can provide improved visualization of surgical fields. Other advantages include simplified skull base closure, reduced risk of CSF leak, and the absence of nasal complications. The major weakness of this approach is the potential problem of limited space for manipulation because of the small bone window.

Surgical Considerations Based on Cyst Location

It is believed that intrasellar RCCs arise between the anterior lobe and pars intermedia, while suprasellar RCCs develop within the pars tuberalis above the diaphragma sellae. Few authors have characterized cyst locations in their studies, and the purely suprasellar RCCs are reported to have a rare occurrence (0–20%). Potts et al. retrospectively reviewed a total of 151 RCCs and reported 19 cases (13%) of suprasellar lesions. They compared the presentations, surgical outcomes, and pathology of lesions with different location, but did not evaluate different surgical approaches according to cyst location and extent of resection. They also claimed that the suprasellar lesions were more difficult to remove via endonasal route and had a higher risk of recurrence, but failed to associate the causes with the surgical approach.

Based on these issues, we believed that individualized surgical strategies should be considered for different RCCs. The key point of approach selection is focused on how to avoid the injury of normal pituitary gland. In general, we typically used endonasal technique to approach intrasellar or intra- and suprasellar RCCs (Fig. 1). Purely suprasellar RCCs, however, were removed by traditional or supraorbital keyhole craniotomy. Due to its more invasive potential, the traditional craniotomy has mainly been replaced by the supraorbital approach since 2006, except for lesions without a clear diagnosis. For the same reason, the extent of resection of the cyst wall was also changed from radical removal to partial removal in transcranial cases. It should be noted that the craniotomy was still used for some intrasellar lesions with suprasellar extension in our series. This is because the residual pituitary gland in these cases is displaced inferiorly and blocks the pathway of the endonasal approach (Fig. 3).

Surgical Techniques

We used the endonasal transseptal technique to approach the sphenoid sinus. This technique is different from a standard endonasal transsphenoidal approach. The advantages are that the nasal mucosa is well preserved, which reduces the risk of iatrogenic nasal complications, and the procedure is much quicker than a standard approach. The transseptal approach has also been successfully used for removal of pituitary adenomas in our institution with favorable outcomes. The major drawback of this approach is limited maneuverability due to the placement of a nasal speculum. However, our experience shows that the working corridor is sufficient for the treatment of RCCs owing to their cystic nature.

To our knowledge, the supraorbital approach has not been used for RCCs by other authors. In our experience, we found this approach to be safe and effective. Preoperative hypopituitarism and DI returned to normal in 100% and 83% of patients who were treated by supraorbital route. However, we have not experienced any new developed hypopituitarism, optic nerve injury, hemorrhage, or meningitis when using this approach. The only patient with postoperative DI after a supraorbital approach recovered to normal within 1 month after surgery. The radiological recurrence rate was also comparable with other series involving patients treated by endonasal technique. Moreover, a fully endoscopic technique was used for 8 recent cases in our series. This technique can provide better visualization, avoid brain retraction, and further reduce invasiveness.

Study Limitations

In this retrospective technique assessment, we described and compared different approaches and the extent of resection for RCCs. There are some limitations to this study, including its retrospective nature. The supraorbital approach was only used since 2006, follow-up was relatively short, and the study size was small. Distribu-
Individualized surgery for Rathke cleft cyst

tion of cyst location and the incidences of some presentations were also unequal between groups. Likewise, an extended endonasal approach was not employed or evaluated for removal of suprasellar cysts. These aspects may to some extent be a reflection of a personal preference regarding the selection of a certain approach; this selection bias, based on both personal and collective experience, evolved over time as different approaches were used. Although our conclusions are logically established based on anatomical location and surgical outcomes, more cases, longer follow-up, and additional surgical modalities are still needed in future study.

Conclusions

Although the endonasal route has been considered the optimal approach for the treatment of RCCs, there are still challenges in the management of purely or mainly suprasellar lesions owing to the location of the normal residual gland in the trajectory of the transsphenoidal corridor or inherent pitfalls of the endonasal route. In this study we have presented a large series of cases involving patients with RCCs treated by transsphenoidal and transcranial approaches, and we conclude that it is reasonable to adopt individualized surgical strategies for RCC based on cyst location. Our results indicate that attempted GTR does not reduce the recurrence rate but does increase the risk of complications. Our experience also suggests that the endonasal approach seems more appropriate for primarily intrasellar RCCs with or without suprasellar extension, whereas the craniotomy is recommended for purely or mainly suprasellar lesions. The supraorbital keyhole route appears to be preferable to traditional craniotomy for its minimal invasiveness and favorable outcomes. Use of endoscopic assistance is recommended for either endonasal or supraorbital keyhole surgery to obtain better visualization and wider exposure.

Acknowledgments

We are grateful to Xiaoyu Qiu and Yiping Mo (Department of Neurosurgery, Nanfang Hospital, Southern Medical University, Guangzhou, China) for their help with the data collection.

Disclosure

This study was financially supported by the Medical Scientific Research Foundation of Guangdong Province (No. B2012219), China. The authors have no other personal financial or institutional interest in any of the drugs, materials, or devices described in this article.

Author contributions to the study and manuscript preparation include the following. Conception and design: Fan. Acquisition of data: Peng, Zhang, Qiu, Pan. Analysis and interpretation of data: Fan, Peng. Drafting the article: Fan. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Qi. Statistical analysis: Zhang. Administrative/technical/material support: Qi. Study supervision: Qi.

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