



Rathke's cleft cysts: a 6-year experience of surgery vs. observation with comparative volumetric analysis

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Abstract

Background Rathke's cleft cysts (RCCs) are common sellar lesions. Their management remains controversial, particularly when small or asymptomatic. Herein we review a consecutive series of RCC patients managed with surgery or observation.

Methods All patients with a new diagnosis of presumed RCC, based on MRI, from February 2012–March 2018 were retrospectively divided into observational and surgical cohorts based on an intent-to-treat model. The cohorts were compared for clinical presentation, and cyst volume. The observational cohort was followed for change in cyst size. The surgical cohort was followed for changes in endocrinopathy, visual symptoms, headache and recurrence.

Results Of 90 patients (mean age 36.7 ± 19.4 years; 68% female), 60% ($n = 54$) were in the observational cohort and 40% ($n = 36$) in the surgical cohort. Average follow-up was 13 ± 23 months in the observational cohort and 24 ± 19 months in the surgical group. In comparing the cohorts, mean ages were similar with more women in the surgical group (81% vs. 56%, $p = 0.04$). Most patients in the observational cohort had incidentally-discovered RCCs ($n = 50$, 88%) as opposed to the surgical cohort ($n = 6$, 17%). The surgical cohort had higher rates of headache (89% vs 26%, $p < 0.001$), endocrinopathy (36% vs 0%, $p < 0.001$), and visual dysfunction (19% vs 0%, $p = 0.001$). Mean cyst volume and maximal cyst dimensions were greater in the surgical cohort (0.94 ± 0.77 cm³ and 14.2 ± 4.1 mm), compared to the observational cohort (0.1 ± 0.14 cm³ and 6.4 ± 3 mm), ($p < 0.001$). Among the 53% ($n = 30/54$) of patients in the observational group with follow-up, 3 (10%) had spontaneous RCC shrinkage, 1 (3%) had modest asymptomatic growth (at 10 months from initial MRI), and 87% had stable cyst size. Of the 36 patients recommended to have surgery, 89% ($n = 32$) did so. Post-operatively, complete or partial resolution of headache, endocrinopathy and visual dysfunction were documented in 90% ($n = 28/30$), 75% ($n = 10/12$), and 100% ($n = 7/7$), respectively. On follow-up MRI, 8 (22%) patients had some cyst reaccumulation, of whom 3 (8%) were symptomatic and underwent uneventful reoperation. No major complications such as hematoma, CSF leak, new endocrinopathy or visual deficits occurred.

Conclusion From this consecutive series, a majority (60%) of RCCs do not appear to warrant surgical intervention and have a low risk of cyst progression. However, surgical cyst removal appears to be indicated and safe for patients with larger, symptomatic RCCs. Simple cyst drainage has a high rate of improvement in pituitary gland function, visual function and headache resolution with low complication rates and symptomatic recurrence risk. These findings stress the importance of careful case selection and potential utility of volumetric assessment for patients with RCCs.

Keywords Endoscopic · Endonasal · Pituitary · Rathke's cleft cyst · Transsphenoidal

Abbreviations

CSF	Cerebrospinal fluid
DI	Diabetes insipidus
GH	Growth hormone
MRI	Magnetic resonance imaging
RCC	Rathke's cleft cyst

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Introduction

Rathke's cleft cysts (RCCs) are non-neoplastic cysts that arise from the remnants of the craniopharyngeal duct of Rathke's pouch during embryogenesis [1–12]. RCCs, also known as pars intermedia cysts, are sellar and/or suprasellar lesions that are typically found between the anterior and posterior lobes of the pituitary gland, but can also arise in a supraglandular location and extend up along the infundibulum [6, 13, 14]. They are relatively common, representing 13–33% of sellar lesions discovered in a large autopsy series, and nearly 1% of intracranial lesions, and account for 7–10% of most large endonasal transsphenoidal surgical series [4, 15–18]. Given the overall increased access to and utilization of imaging, specifically magnetic resonance imaging (MRI), it appears that more RCCs are being detected incidentally [2, 4, 12]. A radiographic study of 2598 patients referred to a tertiary pituitary care center demonstrated a 3% incidence of RCC [19]. Most of these are asymptomatic on discovery, but those that do manifest with symptoms usually demonstrate compressive visual deficits, endocrine dysfunction and/or headaches [4, 8, 11]. The standard treatment of symptomatic RCCs is transsphenoidal cyst fenestration and drainage, however, the management of smaller, seemingly asymptomatic cysts remains somewhat controversial. This study reviews the natural history and surgical versus non-surgical decision making of presumed newly-diagnosed RCCs in a consecutive series of patients evaluated in an outpatient pituitary-disorder clinic.

Methods

Clinical data collection and analysis

All patients presenting to Pacific Neuroscience Institute at Providence Saint John's Health Center in Santa Monica, California, with a radiographically-diagnosed RCC from February 2012–March 2018 were identified. We collected information regarding the patients' demographics, clinical presentation, imaging findings, and outcomes including symptoms and cyst size and morphological change on MRI, complications, and cyst recurrence. Those with RCCs previously operated at outside institutions or those who were diagnosed or managed prior to February 2012 were excluded from our study. The patients were then divided into two groups: observation versus surgery, based on the treatment recommended on initial consultation. Clinical notes, MRIs, pathology reports, laboratory studies, and long-term outcomes were reviewed for each

patient. All patients included in the surgical cohort had pathology findings consistent with an RCC.

All patients' MRIs were carefully reviewed to assess for cyst characteristics, maximal sagittal, axial and coronal dimensions in mm; cyst volume was calculated using the formula $ABC/2$. This volumetric analysis has been validated with segmented volumetric computation for spheroids [20, 21]. All RCCs in this study were spheroid and fit the criteria for this estimation method. In the observational cohort, the diagnosis of RCC was presumed when MRI showed a non-enhancing intra-glandular midline cyst (posterior to the anterior pituitary gland) or a supraglandular non-enhancing midline cyst in contact with the infundibulum [10, 14]. Supraglandular cysts were those defined as being located above the anterior and posterior pituitary gland, as opposed to the more common intraglandular cysts that are situated directly posterior to the anterior pituitary gland. The observational and surgical cohorts were then compared using a Fischer exact test to compare categorical variables and an F-test for continuous variables. A p -value ≤ 0.05 was considered statistically significant.

Surgical decision making

Patients' symptoms, neurological findings, hormonal test results and MRI findings were reviewed and considered. In general, for patients with small cysts (under 1 cm in maximal dimension), surgery was not recommended or offered even in the setting of growth hormone (GH) deficiency, precocious puberty, or headache, unless there was evidence of acute or subacute hemorrhage within the cyst (14 patients in this series, including four with clinical pituitary apoplexy). In contrast, surgery was recommended in patients who had relatively large RCCs (typically over 1 cm in maximal dimension) in the setting of (1) objective chiasmal and/or optic nerve compression with visual field or acuity deficit, or (2) documented hypopituitarism, and/or (3) headache in a typical "pituitary-type" pattern of predominantly midline frontal and nasion distribution, and (4) clinical picture consistent with pituitary apoplexy. Clinical apoplexy is defined as acute-onset of either headaches, hypopituitarism or vision loss along with T1 hyperintensity of RCC. Surgery was also offered in patients with larger lesions in whom the imaging was not entirely classic for RCC and the differential diagnosis included cystic pituitary adenoma or craniopharyngioma.

Surgical technique and post-operative management

As previously described, all patients in the surgical cohort underwent endonasal endoscopic surgery with a team approach by a neurosurgeon and otolaryngologist, initially with a 4-mm 0° rigid endoscope and then with 30° and 45° endoscopes as needed [5, 13, 15, 22–24]. After a standard

approach with mucosal rescue flaps and wide sphenoidotomy, the face of the sella is exposed and removed down to the sellar floor but the sellar floor is not removed. The sellar dura is opened in a low U-shaped fashion and flapped upward with care being taken not to enter the anterior pituitary gland with the initial dural opening. For typical intrasellar RCCs, the cyst contents are immediately posterior to the thinned anterior lobe. Consequently, a low vertical midline gland incision is made with a microblade (in parallel with the vascular supply to the gland) to enter the cyst. To avoid undue traction on the anterior lobe and to facilitate adequate visualization into the cyst cavity, this small window in the inferior aspect of the anterior gland is widened with a small degree of gland resection using micro-scissors [1]. Through this opening, the cyst contents are then removed using suction and, in some cases, ring curettes and cup forceps if solid cyst components are present. Multiple gentle sweeps with the ring curettes along the anterior and posterior lobes and along the lateral walls are made followed by copious gentle saline irrigation into the cavity. A thorough removal is confirmed with a 30° and/or 45° angled endoscope. In an effort to avoid new hypopituitarism, no attempt is made to strip the cyst lining, particularly over the posterior lobe, which is frequently visible after the cyst removal. For supraglandular RCCs (the great majority of which remain infra-diaphragmatic), a somewhat higher bony exposure is needed, though a full transplanum approach is not necessary. Typically, an anterior superior, slightly off-midline gland incision is made to avoid injury to the infundibulum insertion. Using this transglandular approach, these cysts, that often ascend up along the inferior aspect of the infundibulum, can be completely removed [15]. Similarly, for supraglandular RCCs, no attempt is made to strip the cyst lining away from the infundibulum, unless it comes easily without undue traction. Closure and prevention of post-operative cerebrospinal fluid (CSF) leak is performed, as recently described, based on CSF leak grade [16]. In general, nasoseptal flaps are rarely used for RCC patients. Post-operative management involves standard observation for electrolyte abnormalities, acute adrenal insufficiency, and diabetes insipidus (DI). Most patients are discharged home on post-operative day 1 or 2 with an MRI on post-operative day 1 and the next MRI at 3 months post-surgery.

In the surgical cohort, all patients had follow-up visual and pituitary hormonal testing to assess for recovery or deterioration. Specifically, hormonal testing follow-up for each pituitary axis including for DI was assessed at least 3 months post-surgery as previously described [1].

Results

From February 2012 to March 2018, 90 patients with newly-diagnosed presumed RCCs presented to our institution. All patients were diagnosed with RCC based on characteristic

appearance on MRI. Of these patients, 40% ($n = 36$) were recommended to undergo surgical drainage of their cysts, while continued observation with serial MRI was recommended for the remaining 60% ($n = 54$). Over two-thirds of the patients were female ($n = 61$, 68%), with a significantly higher percentage in the surgical cohort compared to the observational group, 81% ($n = 29$) vs. 56% ($n = 32$; $p = 0.04$), respectively.

Table 1 shows patient demographics and clinical presentation of the two groups. Figure 1 includes waterfall plots demonstrating individual patients in the observational and surgical cohorts to compare overall signs and symptoms in relation to RCC volume. Most patients in the observational cohort presented incidentally ($n = 50$, 88%), after an MRI was performed for other reasons such as syncope, sinusitis, or work-up for pediatric GH deficiency, while only 17% ($n = 6$) of patients in the surgical group presented incidentally. Of those in the observational group, 17 (31.5%) presented with short stature and GH deficiency or precocious puberty and the MRI was obtained to rule out any mass lesion that could be the source of the endocrinopathy, 15 (26%) with migraines or other headache complaints, with the remainder presenting with presumably unrelated symptoms such as dysmenorrhea, hirsutism, primary or secondary hypogonadism, acne, obesity, syncope, traumatic brain injury, cancer surveillance, or sinusitis. By contrast, those in the surgical cohort had a higher incidence of headache ($n = 32$, 89%), endocrinopathy ($n = 13$, 36%), compressive visual dysfunction ($n = 7$, 19%), or apoplexy ($n = 4$, 11%). Of the six surgically-treated patients whose RCCs were discovered incidentally, three had MRI evidence of significant gland and/or chiasmal compression, two complained of headaches when questioned in clinic, another two had

Table 1 Demographics, clinical and radiographic presentation

	Observation	Surgery	p-value
Demographics			
Patients (n)	54 (60%)	36 (40%)	
Age (year)	36 ± 21	38 ± 16	0.44
Female gender	32 (56%)	29 (81%)	0.04
Presentation			
Incidental finding	50 (88%)	6 (17%)	< 0.001
Symptoms			
Headache	15 (26%)	32 (89%)	< 0.001
Endocrinopathy	0	13 (36%)	< 0.001
Visual dysfunction	0	7 (19%)	0.001
Radiographic findings			
Cyst volume (cm^3)	0.10 ± 0.14	0.94 ± 0.77	< 0.001
Max cyst dimension (mm)	6.4 ± 3.0	14.2 ± 4.1	< 0.001
Outcomes			
Follow-up (mos)	13 ± 23	24 ± 19	0.008

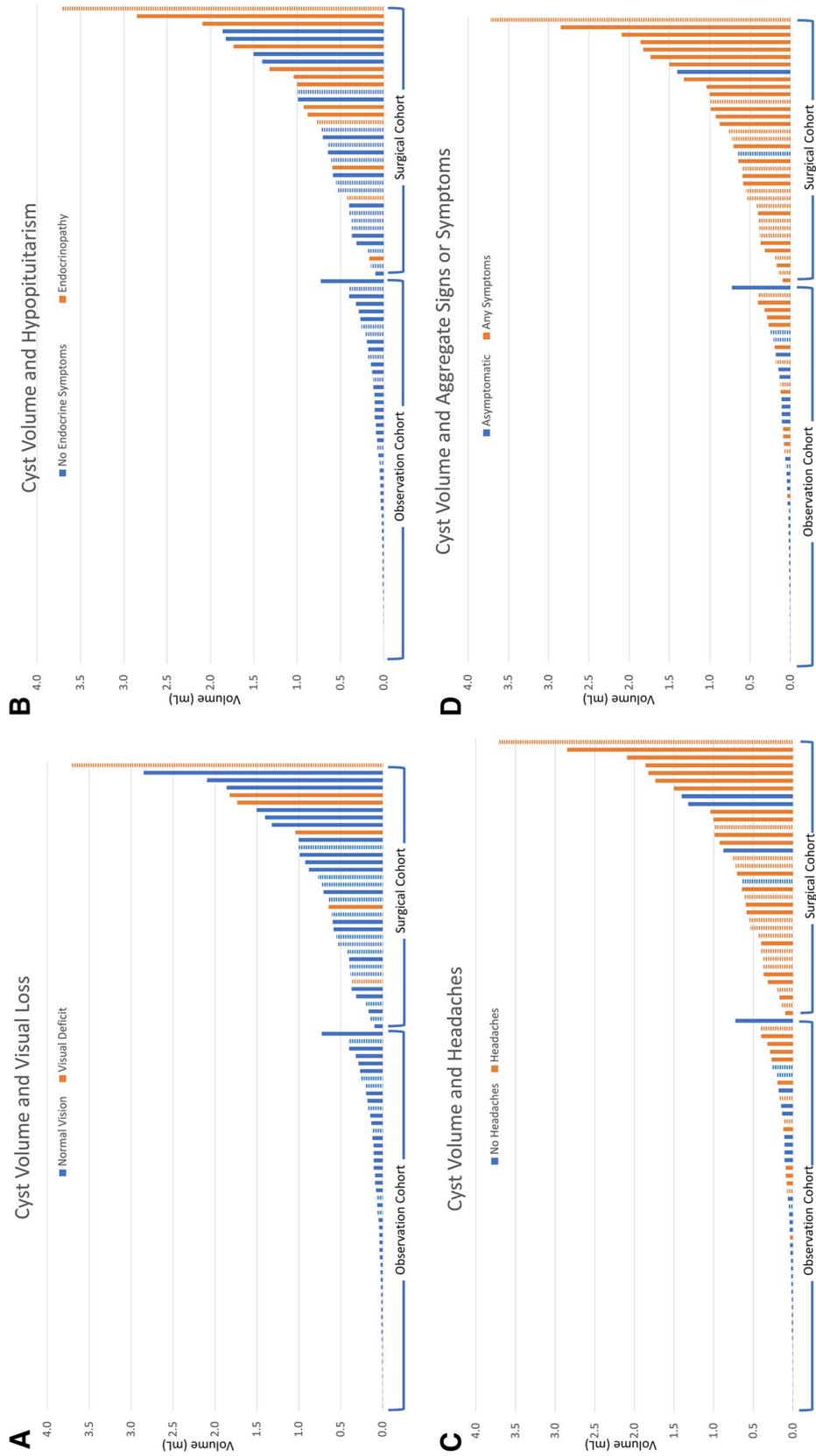


Fig. 1 Scatter plot of surgical versus non-surgical management in 90 patients with RCC based on **a** aggregate signs and symptoms, **b** headaches, **c** hypopituitarism, and **d** visual field defect and/or diminished visual acuity on initial clinical presentation. Patients with supraglandular RCC are denoted with hash-marks

radiographic evidence of hemorrhage within the cyst, and all had cysts greater than 1 cm in greatest dimension. Finally, as shown in Table 1, RCCs in the surgical cohort were significantly larger, with an average volume of $0.94 \pm 0.77 \text{ cm}^3$ and maximal dimension of $14.2 \pm 4.1 \text{ mm}$, compared to those in the observational cohort (volume $0.10 \pm 0.14 \text{ cm}^3$, maximal dimension $6.4 \pm 3.0 \text{ mm}$, $p < 0.001$). Waterfall plots (Fig. 1) show significant differences in frequency and cyst volume across the two cohorts for those presenting with headaches, objective visual field defect and/or visual acuity loss, as well as hypopituitarism. In the subset of pediatric patients whose RCCs were discovered as part of an evaluation for GH deficiency or precocious puberty, cyst volume and maximal dimension averaged 0.079 cm^3 and 6.4 mm , respectively.

In the observational group, follow-up was available for 30 (53%) of 54 patients. Of these, one (3%) patient had evidence of cyst growth without change in symptoms or treatment plan. The other 97% had stable or smaller cysts including 26 (87%) with stable cysts, one (3%) with a smaller cyst and two (7%) with near-complete cyst resolution. Average follow-up for the observational cohort was significantly shorter at 13 ± 23 months compared to the surgical group at 24 ± 19 months ($p = 0.008$). There were no measurable endocrinopathies that developed during the observational period.

Within the surgical cohort, 36 patients for whom surgery was recommended, cyst location was intrasellar and intra-glandular in 22 (61%) and supraglandular, extending along the infundibulum, in 14 patients (39%). Examples of intraglandular and supraglandular RCCs that were managed with observation versus surgery are demonstrated in Fig. 2. There were significantly more supraglandular RCCs in the

surgical cohort ($n = 14$, 39%) compared to the observational cohort ($n = 8$, 16%), $p = 0.014$ (Fig. 1). Of these 36 patients, 4 declined surgery or were lost to follow-up; ultimately 32 patients underwent endoscopic endonasal RCC drainage. There was no significant difference in symptom presentation or surgical outcomes with regards to RCC location (intra-glandular or supraglandular). As shown in Table 2, of these 32 patients, 93% ($n = 28/30$) had improvement in headache, and all patients ($n = 7/7$) had improvement or resolution of their compressive visual symptoms. There was no significant difference in headache resolution with regards to associated vision or endocrine symptoms ($p = 0.28$).

As shown in Table 3, of the 12 patients presenting with endocrinopathy, 75% ($n = 9/12$) had some improvement including 80% ($n = 4/5$) of patients with hypocortisolemia, 50% ($n = 2/4$) of those with secondary hypothyroidism, and 50% ($n = 1/2$) with diabetes insipidus. Stalk-effect hyperprolactinemia resolved in 83% ($n = 5/6$). No patients with GH

Table 2 Outcomes following endoscopic endonasal RCC drainage

	Surgery (n = 32)
Symptom improvement	
Headache	28/32 (88%)
Endocrinopathy	10/12 (83%)
Visual dysfunction	7/7 (100%)
Recurrence	
Radiographic	8 (25%)
Symptomatic	3 (8%)
Return to the OR	3 (8%)

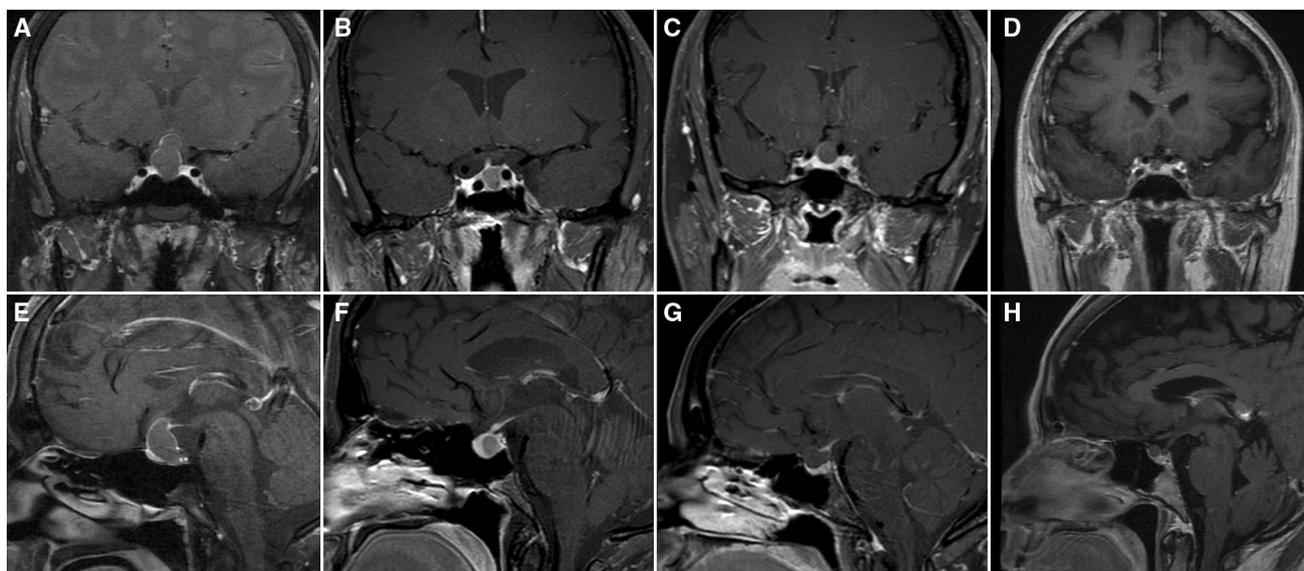


Fig. 2 Coronal and sagittal pituitary protocol MRI images of: **a, b** intraglandular RCC treated surgically; **c, d** intraglandular RCC treated with observation; **e, f** supraglandular RCC treated surgically; **g, h** supraglandular RCC treated with observation

Table 3 Patients presenting with endocrinopathy

Pt	Symptoms	Endocrinopathy												Post-op endocrine change
		ACTH		TSH		GH		FSH		PRL		DI		
		Pre-op	Post-op	Pre-op	Post-op	Pre-op	Post-op	Pre-op	Post-op	Pre-op	Post-op			
1	Asymptomatic			↓	↓									No change
2	Fatigue, weight gain, headache		↓	↑						↑	↓			↑ TSH/free T4, ↓ PRL
3	Fatigue	↓	↑		↓					↑	↓			↑ ACTH/cortisol
4	Amenorrhea, weight gain, galactorrhea				↓					↑	↓			↓ PRL
5	Amenorrhea, difficulty conceiving, weight gain									↑	↓			↓ PRL
6	Headache, amenorrhea, apoplexy									↑	↓			↓ PRL
7	Headache, apoplexy	↓	↑	↓	↓					↓	↓			↑ ACTH/cortisol
8	Diabetes insipidus, headache											Y	N	Resolved DI
9	Headache, bitemporal hemianopsia, apoplexy									↑	↓			↓ PRL
10	Apoplexy	↓	↑	↓	↓									↑ ACTH/cortisol, ↑ TSH/Free T4
11	Apoplexy, headache	↓	↑	↓	↓							Y	Y	↑ ACTH/cortisol
12	Headache, fatigue	↓	↓	↓	↓					↑	↑			No change

deficiency ($n=0/4$) or central hypogonadism ($n=0/3$) had post-operative improvement.

Regarding surgical complications, no patients had a post-operative CSF leak, visual worsening, vascular injury, sellar hematoma requiring a return to the operating room, or new permanent DI or anterior hypopituitarism. Two patients did experience complications with abdominal fat graft harvest site including one hematoma and one seroma, neither of which required re-operation. Ultimately, of 32 patients, 25% ($n=8$) of the surgical cohort had partial cyst reaccumulation on MRI, but only three patients (9%) required re-operation for cyst drainage. Two of these patients were symptomatic with headaches, while the third had a cyst larger than 1 cm in maximal diameter and evidence of radiographic chiasmal compression. All three of these patients with recurrent cysts had uneventful post-operative courses, although one underwent a third resection for a second RCC re-accumulation.

Discussion

In this series of 90 consecutive patients with a presumed RCC, 60% were observed and 40% were offered surgery, of whom 32 ultimately had endonasal endoscopic cyst drainage/removal. Overall surgical outcomes were favorable with headache, endocrinopathy and visual symptoms/signs resolving in 90%, 75% and 100%, respectively. There was no new permanent endocrinopathy or other serious surgical complications, and a relatively low rate of cyst reaccumulation (9%) requiring reoperation, with an average follow-up of 2 years. In the non-surgical cohort, none of the 54 patients progressed to requiring surgery although follow-up in this group was somewhat limited and often of relatively short duration. Below we discuss several important topics related to RCC management, including their natural history and clinical presentation, and most importantly, the surgical selection process and surgical technique to minimize risk of new endocrinopathy.

Natural history

An increasing number of RCCs are being incidentally discovered following MRIs performed for unrelated or non-specific symptoms, such as minor head trauma, metastatic surveillance, headache, and short stature or GH deficiency in children and adolescents. With this trend, the dilemma of how best to manage these largely asymptomatic and incidental lesions has arisen [4].

Several studies have looked into the natural history of RCCs, including Culver, et al. [4] who observed 75 patients with radiographically diagnosed RCCs where 28% of cysts grew on repeat imaging, the rest remained stable or decreased in size, with nearly half of these patients

progressing to surgery. In contrast, our study showed cyst growth in only one patient (3%), and without progression to surgery or new onset symptoms in our observational cohort. The discrepancy can be attributed to a different impetus in recommending surgical removal, or to those patients lost to follow-up in our study, whose cyst growth may have gone undetected. Sanno et al. [25], evaluated 500 patients with incidental sellar lesions, including 94 radiographically-diagnosed RCCs, of which 5.3% of cysts showed growth, but as they remained asymptomatic, could still be followed conservatively. Aho et al. [26] found 160 patients with RCCs over a 12-year period, of which 118 (74%) were symptomatic or became symptomatic on subsequent follow-up with visual impairment or endocrinopathy and underwent surgical cyst drainage, while only 26% ($n=42$) were followed conservatively with serial imaging. The ratio of observational versus surgical patients (26% versus 74%) in the Aho study differs greatly from our own study, of 60% versus 40%, respectively. This large discrepancy in the proportion of patients managed surgically can likely be attributed to a higher rate of MRI scanning in the general population in the present era compared to the Aho study era of 1984–1995, and possibly to modern-day higher resolution MRIs. Regardless, our study certainly makes a case for conservative management in small, asymptomatic, and incidentally-detected RCCs, as none of these patients developed symptoms over time, nor had significant change in cyst size.

The unique aspect of this study, is the careful and detailed dimensional and volumetric comparison of patients in the observational and surgical cohorts, compared for visual field or acuity loss, endocrinopathy, and headache. The resultant waterfall plots clearly show the strong relationship between cyst volume and signs/symptoms, particularly for the objectively-defined visual loss and endocrinopathy. These plots in some ways confirm the obvious, namely that larger cysts (as with larger pituitary adenomas) are much more likely to cause objective vision and endocrine dysfunction as they reach a certain threshold. However, this data while useful, still does not provide strict cut-off RCC volumes for determining which patients should be managed with surgery versus observation. Such decision-making strategy is described below.

Clinical presentation and decision-making

Whether to observe or offer surgery for a RCC should be based on several factors including cyst size and volume, cyst location (supraglandular versus intraglandular), possible evidence of hemorrhage and objective data related to optic apparatus compression, visual field and acuity testing, presence or absence of hypopituitarism, as well as headache information.

The clinical scenario for patients with presumed RCC can be broken down into three subtypes based on size: those with large symptomatic cysts warranting surgery, those with small incidental cysts requiring observation only, and patients with intermediate size cysts, some of whom may necessitate surgery and others who are likely asymptomatic and can be safely observed.

For large symptomatic RCCs, including those typically over 1.5 cm in maximal dimension and causing severe gland compression with endocrinopathy, chiasmal compression with visual impairment, and/or a *clinical* picture of RCC apoplexy, surgery is reasonable and indicated. For relatively small RCCs under 1 cm in maximal dimension, with minimal to moderate gland distortion without endocrinopathy, and no optic apparatus contact, surgery is generally contraindicated regardless of patient symptoms and complaints. Instead, in these patients, observation with repeat MRIs at 6-month intervals for at least 2 years and then annually for up to 5 years may be a more reasonable approach. This strategy is particularly valid given that RCCs have been found in imaging studies in up to 1 in 6 healthy volunteers, and have an incidence of up to 33% of sellar autopsies [6, 18, 27]. The most challenging category is the intermediate size category, including RCCs ranging from approximately 1.0 to 1.5 cm in maximal diameter. In such cases, careful consideration should be given to surgery versus observation. If a classic “pituitary-type” midline headache is present, then surgery may be considered a reasonable option. Although many of our patients in the non-surgical cohort had headaches when queried about their complaints, with an RCC under 1.5 cm in maximal diameter and without bowing of the diaphragm sellae or evidence of hemorrhage, it is unlikely headaches are related to a relatively small RCC. The headaches associated with most RCCs and similar sellar lesions like pituitary adenomas, tend to be midline, frontal-nasion in location and episodic, but occasionally are bilateral or holocephalic [12]. At least one prior study has found that RCC-related headaches typically correlate with high T1-signal, indicative of past hemorrhage or otherwise high protein content and mucinous viscosity [12, 28]. Presence of inflammatory changes on pathology have also been shown to correlate with headaches, though, interestingly, cyst size and compressive endocrinopathy were not shown to be correlative [12]. Visual field deficits and endocrinopathy however, are clearly size and location-related as seen in our findings and other studies [10, 12, 26]. Supraglandular and para-infundibular cysts are expectedly more often associated with DI [10, 12]. Other symptoms such as menstrual irregularities, short stature, and precocious puberty are less likely to be associated with smaller cysts and, as in our series, can be confounding in distinguishing a symptomatic cyst from coincidental symptoms [12, 26].

Surgical technique and complication avoidance

As shown in this small surgical series and several others, when indicated, endoscopic endonasal RCC drainage is safe and effective, with very low complication and recurrence rates. The endoscopic transsphenoidal approach provides direct access to the sella and excellent visualization for effective cyst decompression [1, 11]. As described in the methods and in a prior publication by our group, a low midline anterior gland incision with partial gland resection provides excellent RCC access and allows minimal gland and infundibular manipulation. This method is well-tolerated by the gland with a very low risk of creating new endocrinopathy [1]. DI is the most common complication encountered in the surgical management of RCC. This complication can typically be avoided by not attempting to strip the entire cyst lining, which often stems from or is intimately involved with normal functioning anterior and posterior pituitary gland tissue [9]. Reported rates of permanent DI average around 10%, but can occur in 20% of suprasellar RCCs and up to 40% of cases where aggressive measures are taken to denude the entire lining of the cyst cavity [6, 9–11, 26]. In experienced pituitary centers, and especially with the widespread use of endoscopy in transsphenoidal surgery, CSF leak has become less and less common [16, 22]. Our study saw no incidence of post-operative CSF leak requiring revision or other management with our RCC population, especially with the implementation of a graded intraoperative CSF leak repair protocol [16]. Similarly, most modern and endoscopic studies report very low CSF leak rates from 0 to 2% [9, 11, 16, 26]. Other complications such as new or worsened visual deficits or endocrinopathies are also decidedly rare [6, 9–12, 26]. Ultimately endoscopic endonasal surgical RCC decompression is a relatively low-risk surgery in experienced pituitary centers.

Surgical outcomes and recurrence risk

Following surgical decompression, visual dysfunction has been shown to quickly and robustly recover, in 54–98% of patients, though less so in the case of suprasellar cysts (33%) [3, 6, 10, 11, 26]. Hyperprolactinemia resolved in most, if not all, patients after cyst drainage, while GH deficiency, hypogonadism, hypothyroidism, and hypocortisolemia recovered in less than one-fifth of patients [12, 26]. In our study, hyperprolactinemia similarly improved in most patients, however we also observed a robust recovery in hypocortisolemia post-operatively. Our small study also demonstrated hypothyroidism improvement in half of our patients, though no patients experienced improvement in their hypogonadism or GH deficiency.

Headaches are the most common presentation of RCCs, though seldom are considered a standalone indication for

surgical drainage. Nevertheless, headache improvement has been seen in 71–100% of published reports [6, 12]. Similarly, our study found at least some degree of headache improvement in 90% of patients, such that we feel intractable headaches, with appropriate distribution, especially in the setting of high cyst protein content seen on MRI, should be considered in the initial surgical evaluation of the patient.

Study limitations

The major limitation of this study is its retrospective design with inherent selection bias between the surgical and observational cohorts based on surgeon preference and the patients' presenting symptoms and findings. Clearly, symptomatic patients with large or growing cysts were selected for the surgical arm. Additionally, almost 50% of patients in the observational cohort were lost to follow-up after only one MRI, and as such, growing cysts, or those operated at other facilities would not have been accounted for, possibly underestimating the rate of cyst progression or growth. Moving forward, a carefully designed prospective multicenter registry from pituitary centers of excellence could better address this and similar questions on the natural history of incidentally discovered RCC and pituitary adenomas, as well the surgical indications for such sellar lesions.

Conclusion

A majority of RCCs are asymptomatic incidental findings discovered after radiographic imaging for unrelated indications and do not warrant surgery. Simple surgical cyst drainage appears to be indicated for larger, symptomatic RCCs, especially those presenting with compressive visual deficits, endocrinopathy, or persistent and typical "pituitary-type" headaches. With careful patient selection, an endonasal endoscopic gland-sparing, RCC drainage performed by an experienced pituitary surgery team, has a high rate of symptom improvement with a low incidence of complications.

Compliance with ethical standards

Conflict of interests The authors declare that they have no conflict of interests.

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