



## Clinicopathologic Characteristics and Endoscopic Surgical Outcomes of Symptomatic Rathke's Cleft Cysts

Burak Cabuk<sup>1,3</sup>, Alev Selek<sup>2</sup>, Atakan Emengen<sup>1,3</sup>, Ihsan Anik<sup>1,3</sup>, Zeynep Canturk<sup>2</sup>, Savas Ceylan<sup>1,3</sup>

■ **BACKGROUND:** The purpose of this study was to evaluate the preoperative clinical data and postoperative endocrinologic improvement, recurrence, and complications of Rathke's cleft cysts (RCCs) in a large series of endoscopic transsphenoidal surgery patients, operated in a single center.

■ **METHODS:** Between 1997 and April 2018, 84 patients underwent endoscopic transsphenoidal surgery for RCCs. The presentation symptoms, endocrinologic results by localization and content of the cysts, surgical resections, postoperative complications, and recurrences were evaluated retrospectively.

■ **RESULTS:** Chronic headache was reported in 66.6% (56/84), visual field defects were present in 20.2% (17/84), and 23.8% (20/84) of the cases had pituitary dysfunction. Among the endocrinopathies, 17 of 17 patients had hyperprolactinemia, 2 of 7 patients had cortisol deficiency, and 2 of 13 had hypogonadism, which resolved after surgery. Preoperative pituitary hormone deficiency was associated with gelatinous tumor content ( $P = 0.044$ ). However, there was no significant relationship between tumor localization and preoperative hormone insufficiency. Postoperative hypocortisolemia was seen more frequently in intrasellar RCCs ( $P = 0.048$ ). Three new pituitary hormonal deficiencies were identified in postoperative patients (1 hypocortisolism, 1 diabetes insipidus, 1 hypogonadism). Gross total resection was achieved in 20 cases (23.8%), 9 of which were performed using an extended approach. Postoperative complications included 3 cerebrospinal fluid

leakages and 1 epistaxis. Two patients presented with cyst recurrence at follow-up at 12 and 26 months.

■ **CONCLUSIONS:** Preoperative hormone deficiency was found to be associated with tumor content, independent of size or localization. The surgical aim for symptomatic RCCs should be decompression and this is effective for endocrinologic improvement. An extended endoscopic approach was adequate for total cyst wall removal in suprasellar cysts. Endoscopic transsphenoidal surgery was successful, with low complication rates, for decompression of intrasellar and suprasellar cysts in both complete cyst wall resection and cyst fenestration.

### INTRODUCTION

Rathke's cleft cysts (RCCs) are benign cystic epithelial lesions that may be sellar and/or suprasellar lesions.<sup>1,2</sup> Embryologic development of the hypothalamic-pituitary axis may explain the formation of the cystic epithelial lesions. Rathke's pouch occurs on the 24th day of gestation, as a dorsal diverticulum from the primitive oral cavity, and extends cranially to compose the craniopharyngeal duct. Meanwhile, the infundibulum develops from the diencephalon. Obliteration defects of the craniopharyngeal duct and then inflammatory, metaplastic, and neoplastic processes may occur, resulting in the formation of such lesions, which have a variable clinical spectrum ranging from benign epithelial cysts to aggressive neoplastic craniopharyngiomas.<sup>3</sup> RCCs are usually thought to develop from remnant

#### Key words

- Endoscopy
- Rathke's cleft cyst
- Transsphenoidal

#### Abbreviations and Acronyms

- CSF:** Cerebrospinal fluid  
**DI:** Diabetes insipidus  
**ETS:** Endoscopic transsphenoidal surgery  
**MRI:** Magnetic resonance imaging  
**PRL:** Prolactin  
**RCC:** Rathke's cleft cyst

From the Departments of <sup>1</sup>Neurosurgery and <sup>2</sup>Endocrinology, School of Medicine; and <sup>3</sup>Pituitary Research Center, Kocaeli University, Kocaeli, Turkey

To whom correspondence should be addressed: Savas Ceylan, M.D.  
 [E-mail: [ssceylan@yahoo.com](mailto:ssceylan@yahoo.com)]

Citation: *World Neurosurg.* (2019) 132:e208-e216.

<https://doi.org/10.1016/j.wneu.2019.08.196>

Journal homepage: [www.journals.elsevier.com/world-neurosurgery](http://www.journals.elsevier.com/world-neurosurgery)

Available online: [www.sciencedirect.com](http://www.sciencedirect.com)

1878-8750/\$ - see front matter © 2019 Elsevier Inc. All rights reserved.

cells of the craniopharyngeal duct inside Rathke's pouch.<sup>4-6</sup> Nonetheless, some studies have suggested that RCCs might arise from metaplastic anterior pituitary cells, endodermal cells, or neuroepithelial cells.<sup>7-9</sup>

RCCs are commonly asymptomatic. When they enlarge and cause a mass effect on adjacent structures, they become symptomatic. The recommended management of small, asymptomatic RCCs is follow-up, whereas surgery is indicated for symptomatic RCCs. The typical symptoms of these lesions are headaches, vision, and endocrinologic disturbance.<sup>10-13</sup> The transsphenoidal approach is the surgical method of choice for the treatment of the symptomatic RCCs.<sup>1,14-16</sup> Transsphenoidal fenestration, drainage, and wall resection of RCCs remain the mainstay of treatment.<sup>13</sup> Long-term recurrence rates, after RCC fenestration or resection, have varied from none to 33%.<sup>17-19</sup> Higher rates of recurrence in the literature include inflammation and squamous metaplasia of the cyst wall and superinfection of the cyst.<sup>14,20</sup>

In this study, we present the clinicopathologic characteristics and our experience with 84 patients with RCCs who had sellar-suprasellar RCCs treated by endoscopic transsphenoidal surgery (ETS) and reviewed the surgical outcomes.

## MATERIALS AND METHODS

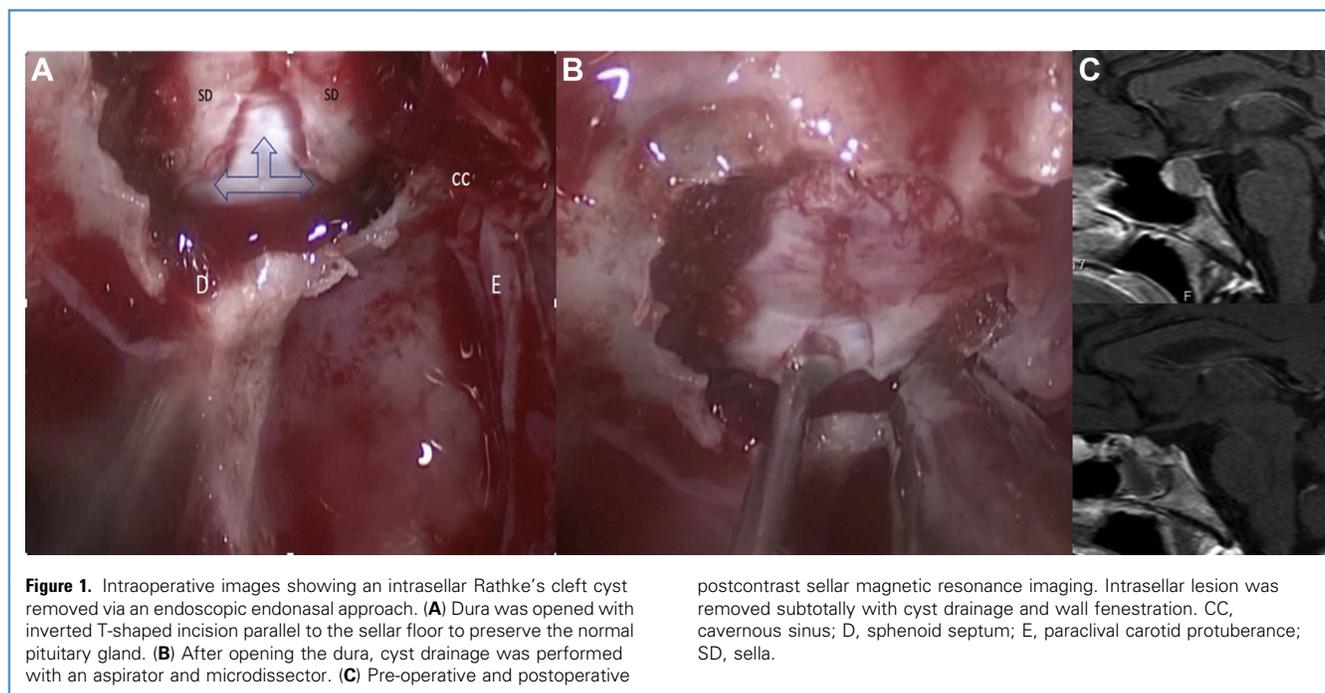
We evaluated 2327 patients who underwent ETS in the Pituitary Research Center and Department of Neurosurgery of Kocaeli University Faculty of Medicine, Turkey, between August 1997 and April 2018. We included the patients who had a sellar lesion in the pituitary gland on magnetic resonance imaging (MRI) and were compatible with RCCs both by the images from the operation videos and histopathologically. None of the patients had a history of previous surgery for RCCs. The concomitant presence of an

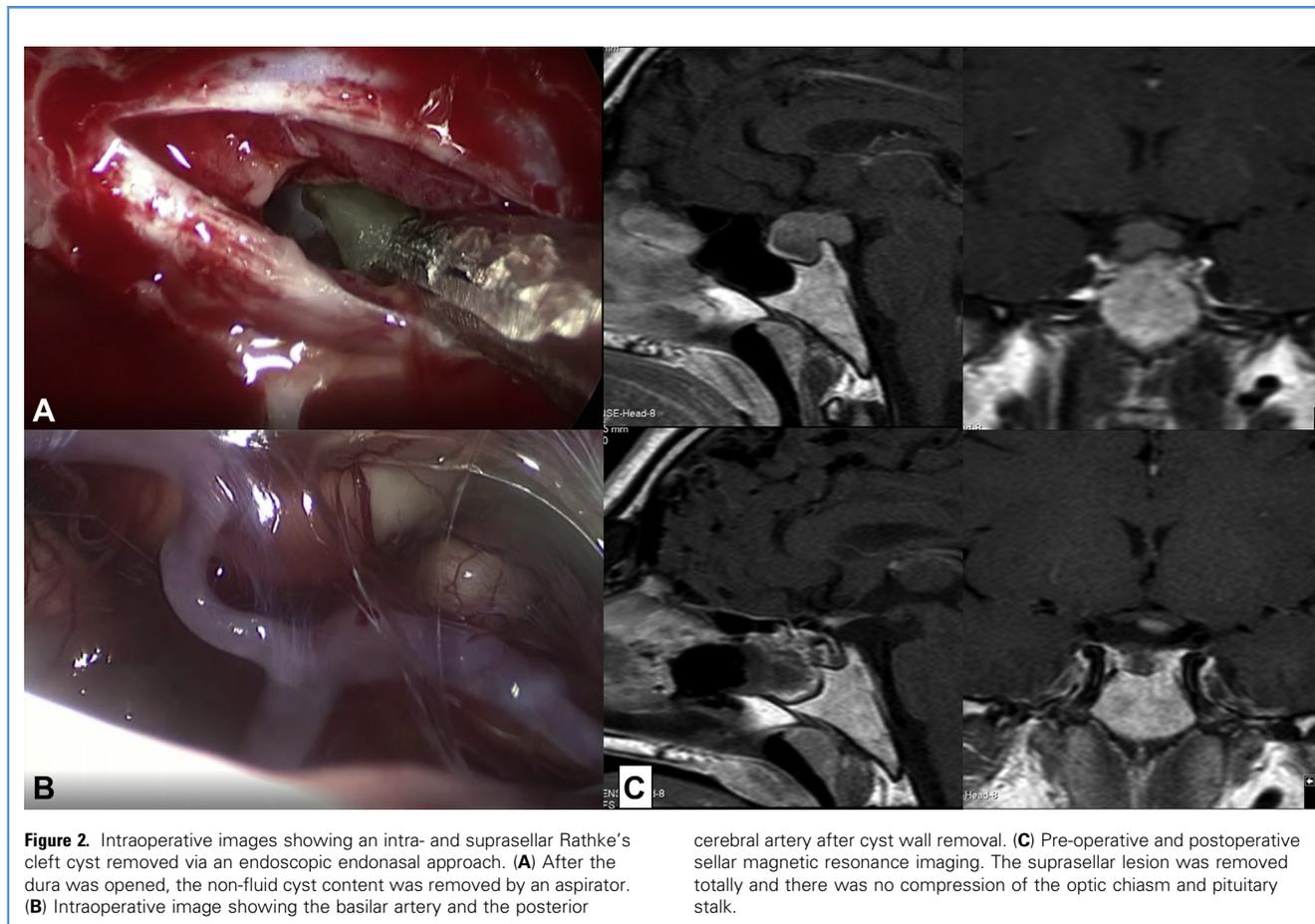
RCC with a second sellar lesion was grounds for exclusion from the present study.

The demographic features, symptoms, complete medical history, and physical examination findings of the patients were evaluated retrospectively from clinical records. The patients' complaints, especially visual field defects, site and severity of headache, and menstrual irregularities, were recorded according to patient description.

Ophthalmologic evaluation was performed preoperatively and at 3 months postoperatively with Humphrey Perimetry for visual field function and Hess Chart Assessment for ocular motility. All patients were also routinely assessed preoperatively and postoperatively at the first 3 days and 3 months by an expert pituitary endocrinologist. Endocrinologic assessments were performed by measurements of the basal and functional pituitary hormone assays including prolactin (PRL), growth hormone, insulin-like growth factor-I, follicle stimulating hormone, luteinizing hormone, testosterone, estradiol, free thyroxine, thyroid stimulating hormone, cortisol, and adrenocorticotropic hormone. Patients were diagnosed as having various endocrine disturbances as follows: secondary hypothyroidism was defined as low free thyroxine in the presence of low or slightly elevated thyroid stimulating hormone levels; hypogonadotropic hypogonadism was defined as low luteinizing hormone, follicle stimulating hormone, testosterone, or estrogen, according to gender. Secondary adrenal insufficiency was diagnosed with low morning cortisol levels (<5 mg/dL) together with symptoms or insufficient cortisol response to adrenocorticotropic hormone stimulation. Hyperprolactinemia was also confirmed with high PRL concentrations, defined as >20 ng/mL for males and >25 ng/mL for females.

Sellar MRI was performed before surgery, and 24 hours and 3 months after surgery. The size, shape, signal intensity, and





location of the lesions were recorded. Preoperative and postoperative sellar MRI sequences, using 1.5 T or 3 T equipment, included precontrast and postcontrast T<sub>1</sub>-weighted images in the sagittal and coronal planes, T<sub>2</sub>-weighted images, dynamic contrast-enhanced T<sub>1</sub>-weighted images in the coronal plane and 3-dimensional volumetric neuronavigation studies. Patients were separated into groups by tumor location on MRI as type I: intrasellar (**Figure 1**), type II: intrasuprasellar (**Figure 2**), or type III: suprasellar (**Figure 3**). Cyst contents were classified by examination of the operation videos and operation notes as either gelatinous, hemorrhagic, inflammatory, or mucinous, as previously described.<sup>21-23</sup> The observational findings were then correlated with pathologic records and MRI reports. In each patient, RCC diagnosis was confirmed by histopathology.

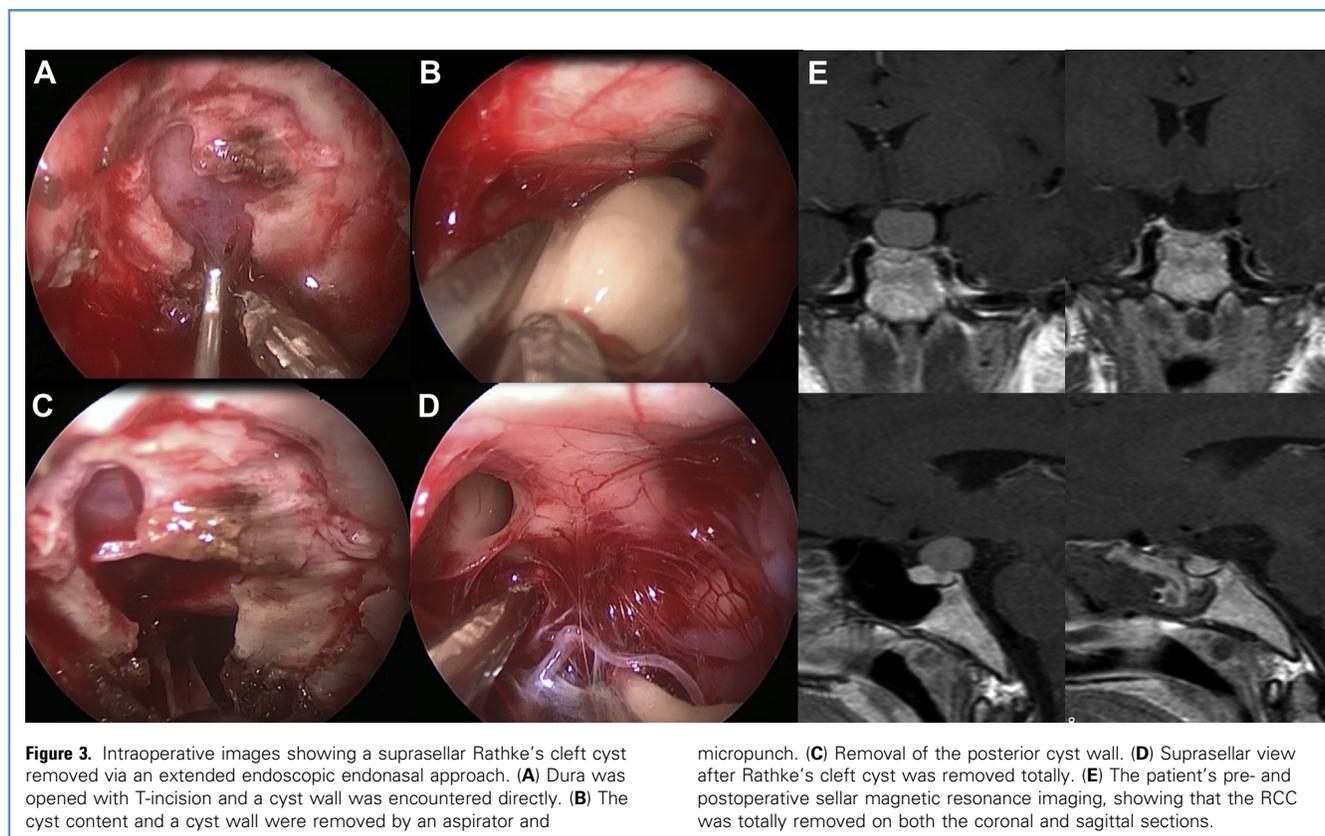
After the 3-month follow-up, patients were followed with MRI and clinical examination annually.

### Surgical Technique

The patients were operated via standard or extended ETS according to the size and location of the epithelial cystic sellar lesion. In order to allow an adequate exposure of the purely suprasellar cystic lesions, an extended endoscopic surgical approach was performed as previously described.<sup>24-26</sup> An inferior standard approach was preferred mostly

for sellar cysts. The surgical approach was chosen based on the location and size of tumor with the aim of draining cyst fluid.

Cysts drainage was performed with an inverted T-shaped dural incision for type I lesions (**Figure 1**). The incision was first made parallel to the sellar floor in the transverse plane and then a second incision in the sagittal plane to preserve the normal pituitary gland. After exposure and incision of the sellar dura, the cyst was exposed and then evacuated and the capsule of the cyst was removed totally or subtotally. When attempting to remove the cyst capsule, we did not perform aggressive surgery in order to prevent damage to surrounding structures, such as the pituitary gland, pituitary stalk, hypothalamus, optic apparatus, and suprasellar cistern, and we allowed a portion of the cyst wall to remain if damage to adjacent structure would have been caused. The patients with purely suprasellar located cysts on preoperative MRI underwent extended endoscopic surgery. If cyst wall dissection was possible with the extended approach, the cyst wall was excised totally. Complete removal of the cyst wall was performed only if it could be achieved without damaging the neural structures and without affecting pituitary functions. Furthermore, cyst walls that had loose connections with adjacent structures and allowed dissection were removed. If there was no cerebrospinal fluid (CSF) leakage during surgery,



we controlled the hemorrhage with absorbable hemostats and no dural repair material was used.

If CSF leak occurred, the sella was repaired by sealing it with fascia and nasoseptal flap. The closure technique that we used for patients who had intraoperative CSF leakage consisted of 3 steps. First, we placed the collagen matrix over the arachnoid membrane and supported it with absorbable hemostat. Afterward, we created a barrier at the dura by compressing the fascia lata graft under the sellar bone and laying the nasoseptal flap on it. In order to combat dural repair defect CSF leakage during the surgery, a lumbar drain was applied to the patients for 5 days.

### Statistical Analysis

All statistical analysis was performed using SPSS for Windows version 20.0 (IBM Inc., Chicago, Illinois, USA) software. Kolmogorov-Smirnov tests were used to test the normality of data distribution. Continuous variables were expressed as mean  $\pm$  standard deviation or median and interquartile range (25th–75th percentiles) as appropriate, and categorical variables were expressed as counts (percentages). Differences between the groups were analyzed by the Mann-Whitney U test, Kruskal-Wallis, 1-way analysis of variance, and Dunn's post hoc test, as appropriate, for numerical variables and the Fisher exact test and Monte Carlo  $\chi^2$  test for categorical variables.  $P < 0.05$  was considered statistically significant for significance.

### RESULTS

Among 2327 patients, 84 (3.5%) patients operated with ETS for RCCs were enrolled into the study. None of the patients had a previous primary operation due to RCCs. The 84 patients included 67 women and 17 men with a mean age of 33.2 years and the age ranged from 12 to 64 years.

Headache, visual field defects, and hormonal disturbances were the most common presenting symptoms. Chronic headache was

**Table 1.** Demographics and Clinical History of Patients with RCCs

	Total	Intra- and Suprasellar		
		Intrasellar	Suprasellar	Suprasellar
Patients	84	31 (36.9%)	46 (54.7%)	7 (8.3%)
Mean age (years)	33.2	34.2	35.2	32.3
Males	17	8	9	0
Symptoms				
Chronic headache	56 (66.6%)	18	34	4
Visual changes	17 (20.2%)	4	11	2
Endocrine dysfunction	20 (23.8%)	7 (8.3%)	11 (13.1%)	2 (2.4%)
RCC, Rathke's cleft cyst.				

**Table 2.** Surgical Results and Recurrence of the RCCs

Surgical approach	Entire Group	Intra- and Intrasellar	Suprasellar	Suprasellar
	Standard approach	72 (85.7%)	31 (36.9%)	40 (47.6%)
Extended approach	12 (14.2%)	0	6 (7.1%)	6 (7.1%)
Contents of the cyst				
Gelatinous	57 (67.5%)	20	31	6
Hemorrhagic	11 (13.1%)	8	3	0
Inflammatory	13 (15.4%)	3	9	1
Mucinous	3 (3.5%)	0	3	0
Type of the resection				
GTR	20	6	9	5
STR	64	25	37	2
Repair of perioperative CSF leaks				
Fascia reconstruction	11	0	8	3
Lumbar drainage	5	0	4	1
Postoperative complications				
CSF leak	3	0	3	0
SIADH	1	0	1	0
Postoperative hormone deficiency	3	0	3	0
Recurrence	2	0	1	1

CSF, cerebrospinal fluid; GTR, gross total resection; RCC, Rathke's cleft cyst; SIADH, syndrome of inappropriate secretion of antidiuretic hormone; STR, subtotal resection.

reported in 66.6% (56/84) of the cases, visual field defects were present in 20.2% (17/84), and 23.8% (20/84) of the cases complained of pituitary dysfunction (Table 1). Distribution of surgical approaches that were performed is shown in Table 2. All operations were performed electively. The mean follow-up of patients was 59 months (range: 3–132 months).

We described subtotal resection as cyst drainage with partial cyst wall removal or biopsy as distinct from gross total resection that consisted of complete cyst content evacuation with total cyst wall removal. In all patients in the subtotal group, a part of the cyst wall was resected for cyst fenestration and served as a biopsy specimen. In our series, gross total resection was performed in 23.8% of cases (20/84), whereas subtotal resection occurred in 76.2% (64/84). Gross total resection was achieved in 9 of 12 (75%) patients who underwent an extended approach (Table 3). The rate of gross total resection in patients with intrasellar cyst was 19.3% (6/31), in patients with intrasuprasellar cyst 19.5% (9/46), and in patients with suprasellar cyst 71.4% (5/7). Data related to the contents of the RCCs are presented in Tables 2 and 3.

After surgery 92.9% (52/56) of patients with headache had complete improvement. It was observed that complete recovery was achieved in 70.5% (12/17) of patients with visual disturbance (Table 4). Hormonal disturbance was diagnosed in 20 (23.8%) of

**Table 3.** Resection Types According to the Surgical Approach

Surgical Approach	Gross Total Resection	Subtotal Resection
Extended (12)	9 (5 ss + 4 iss + 0 is)	3 (1 ss + 2 iss + 0 is)
Standard (72)	11 (0 ss + 5 iss + 6 is)	61 (1 ss + 35 iss + 25 is)
Total (84)	20	64

is, intrasellar; iss, intra- and suprasellar; ss, suprasellar.

the patients in the entire cohort. Among them, hyperprolactinemia was seen in 17 (14.3%) patients and all recovered after surgery. Preoperative cortisol deficiency was observed in 7 (8.3%) patients and 2 of them recovered postoperatively. Preoperative hypogonadism was evident in 13 (15.4%) patients and 2 of them improved postoperatively. Insulin-like growth factor-I levels of the entire group were normal. In 8 (9.5%) patients, there was diabetes insipidus (DI) postoperatively, and one of these was persistent. New hormonal deficiency was seen only in 3 (3.5%) of the patients postoperatively: 1 hypocortisolism, 1 DI, and 1 hypogonadism. We observed 1 patient with transient syndrome of inappropriate secretion of antidiuretic hormone after surgery. Preoperative pituitary hormone deficiency was not associated with tumor size or localization. However, patients with gelatinous tumor content had preoperative pituitary hormone deficiency significantly more frequently ( $P = 0.044$ ) (Table 5). Postoperative cortisol deficiency was seen more frequently in intrasellar RCCs ( $P = 0.048$ ) (Table 6). Hyperprolactinemia was associated with greater tumor size ( $P = 0.048$ ) but not localization (Figure 4). All patients with high preoperative PRL levels recovered postoperatively, whereas new hormonal disturbance was seen in 3 patients. There were no new postoperative visual defects reported.

CSF leak was seen perioperatively in 11 patients and fascia reconstruction was performed to these patients. Five patients underwent perioperative lumbar drainage due to the occurrence of a pressurized CSF leak after extended endoscopic approach surgery. One patient was operated for a second time because of epistaxis. Postoperatively, none of the patients with purely intrasellar cysts developed complications. Postsurgery complications included 3 patients with CSF leaks, all of which were intrasuprasellar cysts and received subtotal resection; 1 patient was treated with an extended approach and the other patients with a standard approach. All of them were operated because of CSF leaks.

Two patients in the subtotal resection group presented with cyst recurrence on MRI at follow-up. The time of recurrence after surgery was 12 and 26 months. Patients were not reoperated because of lack of clinical deterioration.

## DISCUSSION

RCCs are benign cystic that are mostly sellar and sellar/suprasellar. They are rarely confined to suprasellar lesions. During a patient's life, the RCCs may remain stable.<sup>17,27</sup> They become symptomatic because of a mass effect on adjacent structures, such as the pituitary gland, hypothalamus, and optic chiasm, according to lesion size and location. This study analyzed the clinicopathologic characteristics and

**Table 4.** Improvement of Symptoms After Surgery

Symptom	Preoperative (n)	Postoperative Improvement (n)	Percentage Improvement
Chronic headache	56	52	92.9
Visual changes	17	12	70.5

endocrine and surgical outcomes in the largest series of RCCs in our hospital.

Pituitary dysfunction with hypopituitarism and hyperprolactinemia are the most common disorders, and they can be the most pronounced presenting symptom.<sup>5,18,28,29</sup> Hyperprolactinemia was the most common endocrine disturbance in our study, and it was seen more frequently in larger tumors, as expected. However, it was not associated with tumor localization. This may be due to the soft gelatinous content of the tumor as this was the most common type of lesion in the current study. Hyperprolactinemia resolved in all patients, and it is the most common symptom that improves after surgery in our series. After surgery normalized PRL levels might be an additional factor for the improvement of hypogonadism postoperatively.

In contrast, especially in intrasellar tumors, hypocortisolism resolved only in a few patients, compatible with the literature.<sup>28,30</sup> This may be due to the localization of corticotrophs as they are the most numerous in the midsagittal region of the pituitary gland.<sup>31</sup> Therefore, hyperprolactinemia and hypogonadism should be evaluated carefully in patients with RCCs as this may serve as a strong surgical indication. Preoperative hyperprolactinemia was more common in patients with noncyst content.<sup>30</sup> In our study, patients with gelatinous cyst content had higher hormonal deficiency, consistent with the literature.<sup>30</sup>

The surgical indication can be evaluated more accurately with detailed and dynamic tests. In our series, postoperative new hormonal dysfunction and complication rates were lower than some previous reports. New hormonal deficiency was reported in

8% to 12% of patients in the literature; however, only 3.5% of cases in our series experienced new hormonal deficiency. CSF leakage occurred in 3 of our patients (3.5%), which is consistent with the literature reports of the prevalence of around 2% to 7%.<sup>11,12,14,17,32</sup> The postoperative recovery rate of patients with preoperative pituitary dysfunction is higher than those with new hormonal deficiency that develops after surgery. Therefore, in patients with hormonal dysfunction after a good evaluation, surgical treatment may be a better choice. Although it is clear that patients with hyperprolactinemia improved after surgery, we believe that patients with hypocortisolism or hypogonadism should be given the chance to improve with surgery.

Our main goal was to improve the complaints of the patients who underwent surgery and not to cause new hormonal disorders by causing minimal damage to the pituitary gland. Frank et al<sup>8</sup> state that extensive removal of the cyst wall should be carried out only where it is possible without causing additional pituitary damage. Our strategy was as follows: when ETS was performed, after the cyst content was evacuated, gentle resection of the cyst wall should follow, especially when operating on intrasellar and intrasuprasellar RCCs. If the cyst wall is not movable with gentle resection, it should not be removed. However, because of visual defects and severe headache associated with suprasellar RCCs, the cyst should be removed totally with an extended approach. Therefore, gross total resection was achieved in 75% of the patients who underwent extended approach surgery in our series. However, when total excision was performed the complication rate and surgical risk rate increased. One patient developed hypocortisolism in the postoperative period, whereas another patient developed hypogonadism. Fan et al<sup>33</sup> reported that very aggressive treatment resulted in a higher rate of postoperative DI (42%) compared with less aggressive treatment modalities (9%). In our series, 8 patients had DI postoperatively and only 1 patient had persistent DI, the others being transient.

The recommended approach for the treatment of RCCs is transsphenoidal surgery.<sup>14,15,22,34-36</sup> With the widespread use of

**Table 5.** Type of Cyst Content of the RCC with Preoperative and Postoperative Endocrinopathy

	Gelatinous	Hemorrhagic	Inflammatory	Mucinous	P Value
Preoperative endocrine dysfunction, n (%)					0.044*
Hyperprolactinemia	11 (13.1%)	2 (2.3%)	3 (3.5%)	1 (1.1%)	>0.05
Hypocortisolism	5 (5.9%)	1 (1.1%)	1 (1.1%)	0	>0.05
Hypogonadism	9 (10.7%)	1 (1.1%)	2 (2.3%)	1 (1.1%)	>0.05
Postoperative endocrine dysfunction, n (%)					>0.05
Hyperprolactinemia	0	0	0	0	>0.05
Hypocortisolism	4 (4.7%)	1 (1.1%)	1 (1.1%)	0	>0.05
Hypogonadism	8 (9.5%)	1 (1.1%)	2 (2.3%)	1 (1.1%)	>0.05

Postoperative one new hypocortisolism and one new hypogonadism are listed under the postoperative endocrine dysfunction title. The 2 additional new patients, and 4 recovered patients, result in the total number of patients changing by 2.  
RCC, Rathke's cleft cyst.  
\*Preoperative pituitary hormone deficiency was seen more frequently in the patients with gelatinous content.

**Table 6.** Type of the Location of RCC with Preoperative and Postoperative Endocrinopathy

	Intrasellar	Intrasellar + Suprasellar	Suprasellar	P Value
Preoperative endocrine dysfunction, n (%)				>0.05
Hyperprolactinemia	8 (9.5%)	9 (10.7%)	0	>0.05
Hypocortisolism	5 (5.9%)	1 (1.1%)	1 (1.1%)	0.044*
Hypogonadism	6 (7.1%)	7 (8.3%)	0	>0.05
Postoperative endocrine dysfunction, n (%)				>0.05
Hyperprolactinemia	0	0	0	>0.05
Hypocortisolism	5 (5.9%)	0	1 (1.1%)	0.048*
Hypogonadism	6 (7.1%)	6 (7.1%)	0	>0.05

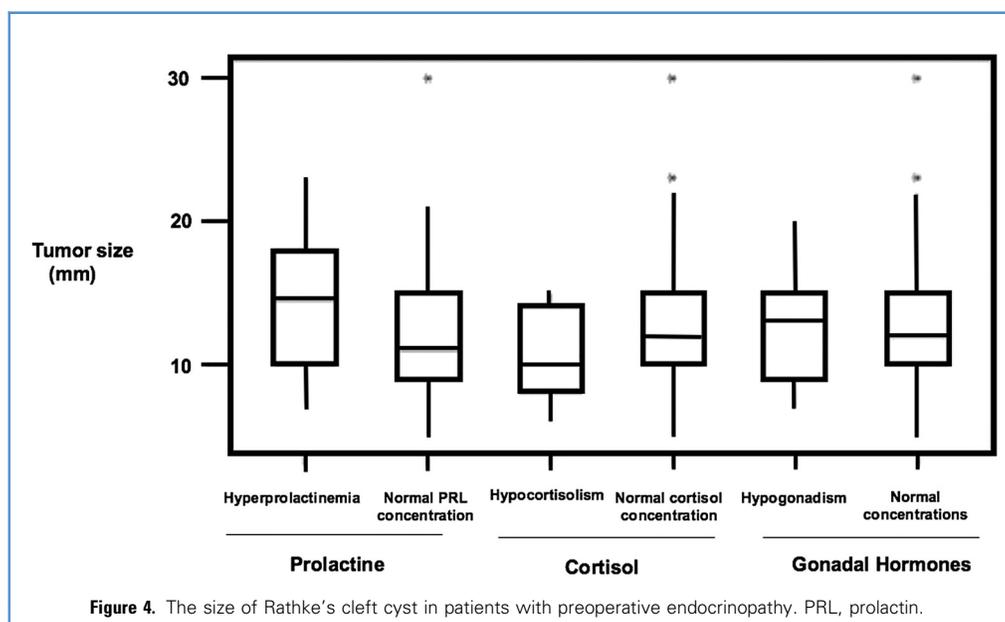
Postoperative one new hypocortisolism and one new hypogonadism are listed under the postoperative endocrine dysfunction title. The 2 additional new patients, and 4 recovered patients, result in the total number of patients changing by 2.

RCC, Rathke's cleft cyst.

\*Statistically significant.

the endoscope, ETS has become a preferable approach for the treatment of RCCs and it has similar results as or better results than the microscopic approach.<sup>21,36</sup> ETS represents a straightforward and minimally invasive approach for carrying out drainage and biopsy of RCCs.<sup>28</sup> Endoscopic surgery provides good surgical manipulation by minimizing pituitary gland damage due to its panoramic view.<sup>6,9,37</sup> In addition, the endoscopic transphenoidal approach has lower recurrence rate and lower rate of postoperative hormonal dysfunctions compared with other approaches.<sup>15,21,29</sup> Although craniotomy is recommended in the treatment of suprasellar RCCs, extended ETS has recently been employed for the management of RCCs of the suprasellar area, as was used in our suprasellar cases.<sup>14,22,34,38-40</sup>

There are few studies comparing the effects of ETS, microscopic surgery, and craniotomy techniques for patients with recurrence. Removing the entire cyst wall may be the main target to prevent recurrence. Many authors have described RCC surgery to involve surrounding tissue decompression with cyst drainage and fenestration of the cyst wall.<sup>4,9,14,15,34,36</sup> The goal of the surgery in our RCC series was to drain the cyst content and, if possible, to remove the cyst capsule safely. Aggressive surgical resection was not preferred for total excision of the cyst capsule. It has been reported that recurrence rate in RCCs was higher in total excision compared with subtotal excisions.<sup>19,21,41,42</sup> Because we encountered a limited number of recurrences after cyst drainage and wall fenestration, our surgical strategy focused on biopsy of the cyst



wall and drainage in treating RCCs. The low rate of recurrence indicated that the subtotal excision was adequate, whereas preserving the pituitary gland and decompression showed significant improvement in the complaints of the patients. As a result, we believe that incomplete removal of the cystic wall is unlikely to cause further pathology and preservation of the pituitary gland is important, as reflected in the good recovery rates of our patients.

We also removed as much of the cyst walls as was possible with careful, atraumatic dissection from the surrounding tissues. When removing the cyst wall, CSF leakage risk increased, because of opening of the suprasellar cistern following aggressive strategies and extended approaches.<sup>15,34,36</sup> We encountered less CSF complications with gentle debulking or with drainage and cyst fenestration. Despite the possibility of the more aggressive strategy causing CSF leakage and damage to surrounding tissues, there is no more benefit for clinical symptoms compared with the less aggressive surgery with cyst decompression. However, it is still not possible to determine the most effective surgical strategy without evaluating the localization, size, content, and histologic features of the cyst.

This study has some limitations that should be noted. The limited follow-up period, with a mean follow-up duration of 59 months, of the 84 patients is the main handicap of this study in terms of assessing recurrence risk. Large series with longer term follow-up are needed to confirm the recurrence rates with the less

aggressive endoscopic technique. Furthermore, we could not determine whether there was a different cause of recurrence other than due to subtotal resection in the patients who had recurrence.

## CONCLUSIONS

The improvement in pituitary dysfunction emphasizes the importance of surgery in the management of RCCs. Subtotal resection is sufficient for endocrinologic improvement with low recurrence and complication rates. Development of new hormonal insufficiency after surgery was less in our cohort than has previously been reported. Tumor content is associated with preoperative hormone deficiency, rather than localization and size. In suprasellar RCCs, the tumor should be removed completely using an extended approach, if possible, because of the associated visual impairment and severe headache. Our data supported a less aggressive endoscopic surgical technique for better endocrinologic outcomes in RCC treatment.

## ACKNOWLEDGMENTS

The authors are grateful to Jeremy Jones of the Academic Writing Department of Kocaeli University, Izmit, Turkey, for his assistance in editing the English used and for his help and advice concerning the contents of this manuscript.

## REFERENCES

- Laws ER. Endoscopic surgery for cystic lesions of the pituitary region. *Nat Clin Pract Endocrinol Metab.* 2008;4:662-663.
- Matsushima T, Fukui M, Fujii K, Kinoshita K, Yamakawa Y. Epithelial cells in symptomatic Rathke's cleft cysts. A light-and electron-microscopic study. *Surg Neurol.* 1988;30:197-203.
- Zada G, Lin N, Ojerholm E, Ramkissoon S, Laws ER. Craniopharyngioma and other cystic epithelial lesions of the sellar region: a review of clinical, imaging, and histopathological relationships. *Neurosurg Focus.* 2010;28:E4.
- Lanelli A, Martini C, Cosottini M, Castagna M, Bogazzi F, Muscatello L. Rathke's cleft cysts in children: clinical, diagnostic, and surgical features. *Childs Nerv Syst.* 2012;28:297-303.
- Voelker JL, Campbell RL, Muller J. Clinical, radiographic, and pathological features of symptomatic Rathke's cleft cysts. *J Neurosurg.* 1991;74:535-544.
- Wen L, Hu LB, Feng XY, et al. Rathke's cleft cyst: clinicopathological and MRI findings in 22 patients. *Clin Radiol.* 2010;65:47-55.
- Hirano A, Ghatak NR, Wisoff HS, Zimmermann HM. An epithelial cyst of the spinal cord: an electron microscopic study. *Acta Neuropathol.* 1971;18:214-223.
- Hirano A, Hirano M. Benign cystic lesions in the central nervous system. Light and electron microscopic observations of cyst walls. *Childs Nerv Syst.* 1988;4:325-333.
- Shuangshoti S, Netsky MG, Nashold BS Jr. Epithelial cysts related to sella turcica. Proposed origin from neuroepithelium. *Arch Pathol.* 1970;90:444-450.
- Cote DJ, Besasie BD, Hulou MM, Yan SC, Smith TR, Laws ER. Transsphenoidal surgery for Rathke's cleft cyst can reduce headache severity and frequency. *Pituitary.* 2016;19:57-64.
- Langlois F, Manea A, Lim DST, et al. High prevalence of adrenal insufficiency at diagnosis and headache recovery in surgically resected Rathke's cleft cysts—a large retrospective single center study. *Endocrine.* 2019;63:463-469.
- Wait SD, Garrett MP, Little AS, Killory BD, White WL. Endocrinopathy, vision, headache, and recurrence after transsphenoidal surgery for Rathke cleft cysts. *Neurosurgery.* 2010;67:837-843.
- Zhong W, You C, Jiang S. Symptomatic Rathke cleft cyst. *J Clin Neurosci.* 2012;19:501-508.
- Benveniste RJ, King WA, Walsh J, Lee JS, Naidich TP, Post KD. Surgery for Rathke cleft cysts: technical considerations and outcomes. *J Neurosurg.* 2004;101:577-584.
- Cavallo LM, Prevedello D, Esposito F, et al. The role of the endoscope in the transsphenoidal management of cystic lesions of the sellar region. *Neurosurg Rev.* 2008;31:55-64.
- Lin M, Wedemeyer MA, Bradley D, et al. Long-term surgical outcomes following transsphenoidal surgery in patients with Rathke's cleft cysts. *J Neurosurg.* 2018;130:831-837.
- Aho JY, Liu C, Zelman V, Couldwell WT, Weiss MH. Surgical outcomes in 118 patients with Rathke cleft cysts. *J Neurosurg.* 2005;102:189-193.
- El-Mahdy W, Powell M. Transsphenoidal management of 28 symptomatic Rathke's cleft cysts, with special reference to visual and hormonal recovery. *Neurosurgery.* 1998;42:7-17.
- Kim JE, Kim JH, Kim OL, et al. Surgical treatment of symptomatic Rathke cleft cysts: clinical features and results with special attention to recurrence. *J Neurosurg.* 2004;100:33-40.
- Tate MC, Jahangiri A, Blevins L, Kunwar S, Aghi MK. Infected Rathke cleft cyst: distinguishing factors and factors predicting recurrence. *Neurosurgery.* 2010;67:762-769.
- Mendelson ZS, Husain Q, Elmoursi S, Svider PF, Eloy JA, Liu JK. Rathke's cleft cyst recurrence after transsphenoidal surgery: a meta-analysis of 1151 cases. *J Clin Neurosci.* 2014;21:378-385.
- Potts MB, Jahangiri A, Lamborn KR, Blevins LS, Kunwar S, Aghi MK. Suprasellar Rathke cleft cyst: clinical presentation and treatment outcomes. *Neurosurgery.* 2011;69:1058-1068.
- Solari D, Cavallo LM, Somma T, et al. Endoscopic endonasal approach in the management of Rathke's cleft cysts. *PLoS One.* 2015;10:10.
- Cappabianca P, Frank G, Pasquini E, de Divitiis O, Calbucci F. Extended endoscopic endonasal transsphenoidal approaches to the suprasellar region, planum sphenoidale and clivus. In: de Divitiis E, Cappabianca P, eds. *Endoscopic Endonasal Transsphenoidal Surgery.* Wien, Austria: Springer-Verlag; 2003:176-187.

25. Cavallo LM, Messina A, Cappabianca P. Endoscopic endonasal surgery of the midline skull base: anatomical study and clinical considerations. *Neurosurg Focus*. 2005;9:E2.
26. Ceylan S, Koc K, Anik I. Extended endoscopic approaches for midline skull-base lesions. *Neurosurg Rev*. 2009;32:309-319.
27. Sala E, Moore JM, Amarin A, et al. Natural history of Rathke's cleft cysts: a retrospective analysis of a two centers experience. *Clin Endocrinol*. 2018;89:178-186.
28. Frank G, Sciarretta V, Mazzatenta D, Farneti G, Modugno GC, Pasquini E. Transsphenoidal endoscopic approach in the treatment of Rathke's cleft cyst. *Neurosurgery*. 2005;56:124-128.
29. Midha R, Jay V, Smyth HS. Transsphenoidal management of Rathke's cleft cysts: a clinicopathological review of 10 cases. *Surg Neurol*. 1991;35:446-454.
30. Oyama N. Assessment of pre and postoperative endocrine functions in 94 patients with Rathke's cleft cyst. *Endocr J*. 2013;60:207-213.
31. Soto-Rivera CL, Majzoub JA. Adrenocorticotrophic hormone. In: Melmed S, ed. *The Pituitary*. 4th ed. Academic Press; 2017:47-83.
32. Higgins DM, Van Gompel JJ, Nippoldt TB, Meyer FB. Symptomatic Rathke cleft cyst: extent of resection and surgical complications. *Neurosurg Focus*. 2011;31:E2.
33. Fan J, Peng Y, Qi S, Zhang XA, Qiu B, Pan J. Individualized surgical strategies for Rathke cleft cyst based on cyst location. *J Neurosurg*. 2013;119:1437-1446.
34. Lillehei KO, Widdel L, Astete CA, Wierman ME, Kleinschmidt-DeMasters BK, Kerr JM. Transsphenoidal resection of 82 Rathke cleft cysts: limited value of alcohol cauterization in reducing recurrence rates. *J Neurosurg*. 2011;114:310-317.
35. Park JK, Lee EJ, Kim SH. Optimal surgical approaches for Rathke cleft cyst with consideration of endocrine function. *Neurosurgery*. 2012;70:250-256 [discussion: 256-257].
36. Teramoto A, Hirakawa K, Sanno N, Osamura Y. Incidental pituitary lesions in 1000 unselected autopsy specimens. *Radiology*. 1994;193:161-164.
37. Madhok R, Prevedello DM, Gardner P, Carrau RL, Snyderman CH, Kassam AB. Endoscopic endonasal resection of Rathke cleft cysts: clinical outcomes and surgical nuances. *J Neurosurg*. 2010;112:1333-1339.
38. Couldwell WT, Weiss MH. *Pituitary Disorders*. Baltimore, MD: Lippincott Williams & Wilkins; 1999.
39. Kanter AS, Sansur CA, Kane JA Jr, Laws ER Jr. Rathke's cleft cyst. *Front Horm Res*. 2006;34:127-157.
40. Koutourousiou M, Grotenhuis A, Kontogeorgos G, Seretis A. Treatment of Rathke's cleft cysts: experience at a single centre. *J Clin Neurosci*. 2009;16:900-903.
41. Chotai S, Liu Y, Pan J, Qi S. Characteristics of Rathke's cleft cyst based on cyst location with a primary focus on recurrence after resection. *J Neurosurg*. 2015;122:1380-1389.
42. Kinoshita Y, Tominaga A, Usui S, et al. The long-term recurrence of Rathke's cleft cysts as predicted by histology but not by surgical procedure. *J Neurosurg*. 2016;125:1002-1007.

*Conflict of interest statement: The authors declare that the article content was composed in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.*

*Received 31 May 2019; accepted 24 August 2019*

*Citation: World Neurosurg. (2019) 132:e208-e216.*

*<https://doi.org/10.1016/j.wneu.2019.08.196>*

*Journal homepage: [www.journals.elsevier.com/world-neurosurgery](http://www.journals.elsevier.com/world-neurosurgery)*

*Available online: [www.sciencedirect.com](http://www.sciencedirect.com)*

*1878-8750/\$ - see front matter © 2019 Elsevier Inc. All rights reserved.*