



## Pineal Cyst–Related Aqueductal Stenosis as Cause of Intractable Headaches in Nonhydrocephalic Patients

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■ **BACKGROUND:** Pineal cysts (PCs) are histologically benign lesions of the pineal gland. Although the majority of PCs are asymptomatic, some cases are ambiguous and accompanied by nonspecific symptoms of variable severity. We suggested that disabling headache in nonhydrocephalic patients with PCs is associated with cerebral aqueduct (CAq) stenosis.

■ **METHODS:** A retrospective analysis was conducted in patients with PCs suffering from headache without secondary hydrocephalus who underwent surgical resection at Burdenko Neurosurgery Center between 1995 and 2016. All available medical records and radiographic images were retrospectively assessed in these patients. The comparison groups included 22 patients with nonoperated PCs and 25 healthy individuals. Specific magnetic resonance imaging measures were selected to assess the morphometry of the CAq and degree of the stenosis.

■ **RESULTS:** In 25 patients (82%) we observed clinical improvement after surgery in a follow-up period. Among those with improvement, 10 of them (40%) experienced total relief and 15 of them (60%) had marked headache diminishment. In 5 patients the headache remained persistent. The preoperative rostral CAq diameter appeared to be significantly narrower ( $P = 0.0011045$ ), and the preoperative rostral/caudal diameter ratio (Rd/Cd) was found to be lower ( $P = 0.004391$ ) in patients who recovered from headache versus those who did not.

■ **CONCLUSION:** The results indicate a statistically significant relationship between the changes in the CAq

morphometrics and the clinical outcome in postoperative period. Surgical removal of symptomatic pineal cysts in patients without hydrocephalus can be considered as an effective treatment. However, a thorough preoperative examination and patient selection should be conducted in every case.

### INTRODUCTION

Pineal cysts (PCs) are histologically benign lesions of the pineal gland. Understanding the natural history of pineal cysts has been challenging and is not well defined despite their high prevalence. According to magnetic resonance imaging (MRI) studies, the prevalence of PCs in the general population is close to 10% with a female predominance, while postmortem examination shows a 40% epidemiologic incidence.<sup>1-6</sup>

The majority of pineal cysts are incidental findings and usually are not related to symptoms that are presented in patients who are seeking medical help. In rare cases PCs can manifest with secondary hydrocephalus due to cerebral aqueduct (CAq) occlusion or Parinaud syndrome. Such conditions are straightforward indications for PC surgical treatment.<sup>7-10</sup>

Even though a high prevalence of PCs exists in the population, the clinical approach to symptomatic PCs accompanied with nonspecific symptoms without obvious evidence of cerebrospinal fluid (CSF) obstruction and with tectal compression is still highly controversial to date.<sup>11</sup> Disabling headache, dizziness, nausea, episodic loss of consciousness are thought to be nonspecific to PCs.<sup>11,12</sup> There is no consensus among neurosurgeons regarding indications for surgery in these disputable cases. Although some

#### Key words

- Cerebral aqueduct
- Headache
- Neurosurgery
- Magnetic resonance imaging
- Pineal cyst

#### Abbreviations and Acronyms

- Avg:** Average  
**CAq:** Cerebral aqueduct  
**CSF:** Cerebrospinal fluid  
**PC:** Pineal cyst  
**Rd/Cd ratio:** Rostral/caudal diameter ratio

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authors advocate that in the absence of hydrocephalus headache should not be related to pineal cyst, others advocate surgery, assuming that the causative factor for it might be the intermittent obstruction of the aqueduct or compression of deep venous collectors such as internal cerebral veins.<sup>13-17</sup>

In this study, we conducted a retrospective review to examine the clinical outcomes of surgically treated symptomatic individuals with PC in the absence of hydrocephalus. Our main hypothesis was that disabling headache in patients with nonhydrocephalic PCs is associated with partial CAq stenosis.

## MATERIALS AND METHODS

### Population

Between 1995 and 2016, 101 patients with symptomatic pineal cysts underwent surgical resection at the Burdenko Neurosurgery Center. Thirty-five patients with secondary hydrocephalus were excluded from the study. Also, 16 patients with asymptomatic PC in the absence of hydrocephalus who underwent surgeries due to the PC imaging characteristics resembling tumor did not meet inclusion criteria. Of the remaining 50 patients, we were unable to follow up 20 of them in a long-term period for different reasons. A total of 30 patients with headache and without hydrocephalus were available for evaluation in a long-term follow-up period. The male-to-female ratio was 1:3 (7 males, 23 females); the median age was 25, ranging from 5–52 years. All available medical records and MR imaging were retrospectively evaluated in these patients. Their

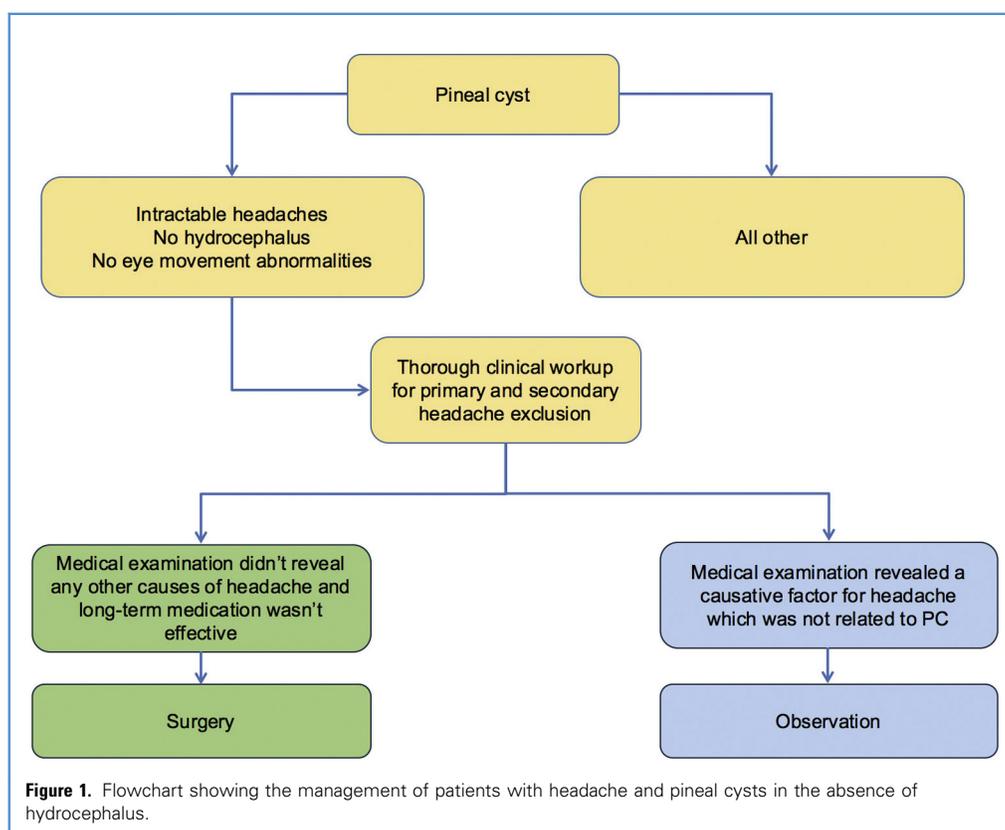
symptoms, cyst size, the presence of ventriculomegaly (Evan's ratio) on preoperative MRI scans, morphometrics of the CAq, surgical approach, and clinical outcome were reviewed.

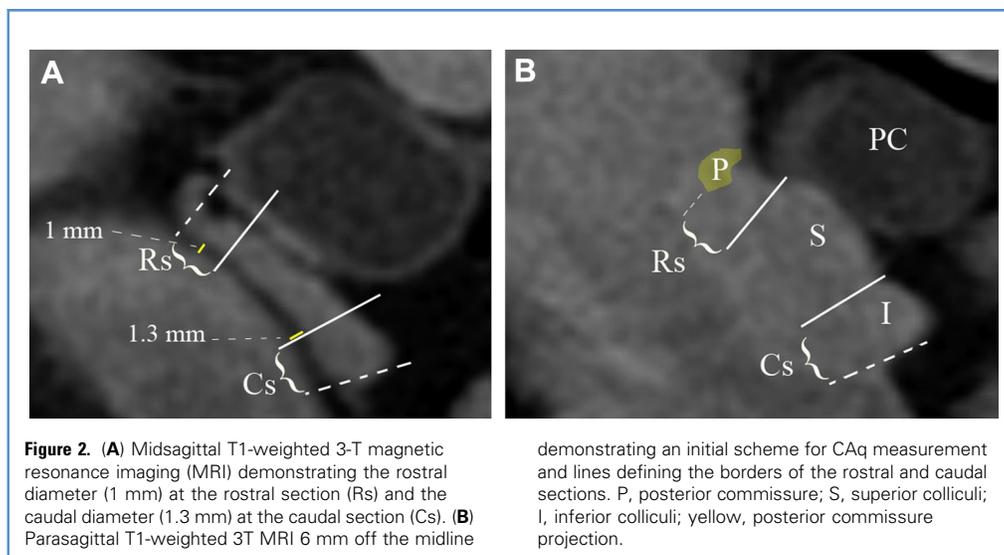
Two comparison groups were included in this study: the reference group and a group of patients with PCs without surgical treatment. In the reference group we included 25 individuals who underwent MRI screening for different reasons and to whom no brain pathology was eventually found. The male-to-female ratio in the reference group was ~1:1 (11 male, 14 female), and the median age was 28 years, ranging from 9–54 years.

The group of patients with PCs who did not undergo any surgical treatment were followed up between 2009 and 2017 ( $n = 22$ ). The male-to-female ratio in this group was 1:5 (4 males, 18 females), and the median age 28, ranging from 4–41 years.

### Clinical Examination and Selection for Surgery

All patients underwent a thorough medical workup (Figure 1). None of them were offered surgery as a first choice of treatment on their first visit to the hospital. Preoperative symptoms were documented and evaluated for any variations before offering surgery. All patients underwent precise examination by an experienced neurologist for exclusion of other conditions associated with headache. In addition, 28 of 30 patients (93%) were evaluated by the Headache Impact Test 6 (HIT-6)<sup>18</sup> for assessment of the headache impact on their everyday life. In the remaining 2 patients, the headache impact test was not applicable before surgery as 1 of them was operated on in 1995





and another patient was a 5-year-old child. The severity of headache was evaluated using the following 4-impact grade scale based on the obtained HIT-6 score: little to no impact (HIT-6 score: 36–49), moderate impact (HIT-6 score: 50–55), substantial impact (HIT-6 score: 56–59), and severe impact (HIT-6 score: 60–78). Headaches associated with different types of migraine, tension type, and cluster headaches were considered as nonindicative for surgery. The presence of ambiguous inexplicable debilitating headache refractory to medication was the subject for surgery.

### Magnetic Resonance Imaging

The CAq morphometric data in the reference group was primarily reviewed in order to compare it with CAq measurements in patients with PCs.

We retrospectively reviewed unenhanced T1-weighted images in 25 individuals without any brain pathology. Accurate morphometrics of CAq were obtained in these subjects using high-resolution magnetic resonance imaging (MRI) on a 3-T magnet (Signa 3.0 HDxt, GE Healthcare, Chicago, Illinois, USA). The scans were performed with a high-resolution imaging protocol (3D T1-WI SPGR) in the axial plane (slice thickness, 1.0–1.2 mm; repetition time 8.3 msec; echo time, 3.5 msec; matrix, 512 × 512) with following sagittal and coronal reconstruction.

Regarding the group with PCs, each case was carefully assessed. The best suitable midsagittal T1-weighted MRI from the 3-T and 1.5-T MRI were chosen for the morphometric assessments with 1-mm slice thickness. The anterior-posterior and craniocaudal cyst sizes were determined using the largest diameters on a midsagittal MRI. The largest transverse cyst size was determined using the largest diameter on a coronal MRI.

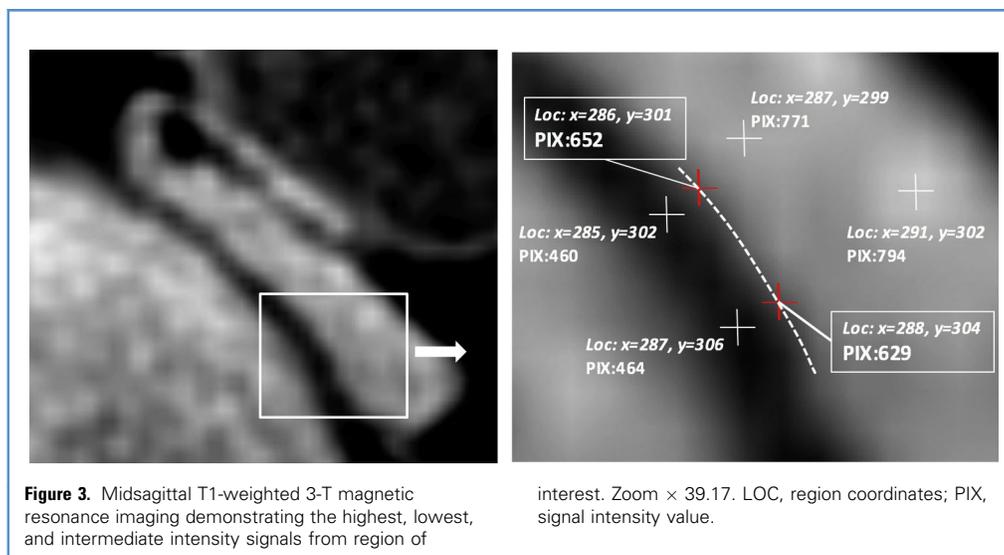
The specific MRI measures were selected to assess morphology of the CAq and the degree of stenosis.<sup>19</sup> For each individual the diameters of the CAq were measured in the rostral and caudal sections (Figure 2). The rostral section of the CAq was defined by a space lying between a line intersecting caudal aspect of the posterior commissure and a line intersecting the

superior border of the superior colliculus. The caudal section of the CAq extended from a line intersecting the superior border of the inferior colliculus to its caudal border. The diameters were measured in the sagittal plane, perpendicular to the long axis of the CAq. The rostral diameter (Rd) was measured at the narrowest point of the rostral section or at its middle area. The caudal diameter (Cd) was measured at the level of the superior border of the inferior colliculus. Occasionally, the clear demarcation border between the CSF and brain tissue could not be identified on MRI scans. This occurs mainly due to the thickness of MRI slice exceeding the measured diameters of the CAq and may alter the values of measurements. Nevertheless, high contrast between CSF and brain tissue can be distinguishable within a voxel under high magnification. For differentiation of zones of superimposed signals, we first evaluated the signal intensity values from different areas at the region of interest: brain tissue around CAq and CSF. The highest signal intensity value from brain tissue and the lowest value from CSF were defined. The borders of the CAq lying within the intermediate zone were identified as an approximation to the arithmetic mean of the highest signal intensity value from brain tissue and the lowest signal intensity value from CSF (Figure 3).

A rostral-to-caudal diameters ratio (Rd/Cd) was further defined as the ratio between rostral and caudal diameters in the same midsagittal plane. This parameter was calculated before and after surgery to assess its dynamics. The morphometrics and their ratios described earlier were selected because they could be easily applied for assessment of the relationship between postoperative clinical outcome and initial CAq morphometry altered by PC compression.

### Follow-Up

Assessment of symptoms, surgery outcomes, and MRI scans were performed independently.



In the follow-up period each patient was interviewed and evaluated by 2 different neurosurgeons, and all symptoms were documented. The second step included neurologic and ophthalmologic examination. Neurologic symptoms, particularly the severity of headaches, were evaluated and compared by neurologist with the preoperative baseline data. Headache severity was reassessed by HIT-6 and compared with the preoperative score. Preoperative and postoperative MRI were obtained and compared in all cases in order to exclude the presence of any residual or recurrent cyst.

### Statistical Analysis

The study was designed as an observational cohort data analysis. The continuous variables were presented as mean and standard deviation (SD). Counts and percentages were used for description of categorical variables. The differences in CAq diameters and CAq diameter ratios between 2 samples were assessed with the nonparametric Mann-Whitney U-test. Categorical variables in subgroups were compared applying the Fisher exact test and chi-square test. The Spearman correlation coefficient was used to assess the correlation between 2 continuous variables.  $P < 0.05$  was considered statistically significant. The analysis scenario and all the statistical calculations were performed using the R programming language (version 3.3.2, 2016, [www.r-project.org](http://www.r-project.org)) in RStudio IDE.

## RESULTS

### Presenting Symptoms

Preoperative symptoms included headache ( $n = 30$ ), dizziness ( $n = 15$ ), diplopia ( $n = 5$ ), and episodic loss of consciousness ( $n = 4$ ). A tension-type headache was persistent in 27 cases and intermittent in 3. The HIT-6 score showed moderate impact ( $n = 2$ ), substantial impact ( $n = 22$ ), and severe impact ( $n = 4$ ). The preoperative ophthalmologic symptoms were associated with

pupillary dysfunction ( $n = 10$ ), and none presented with Parinaud syndrome.

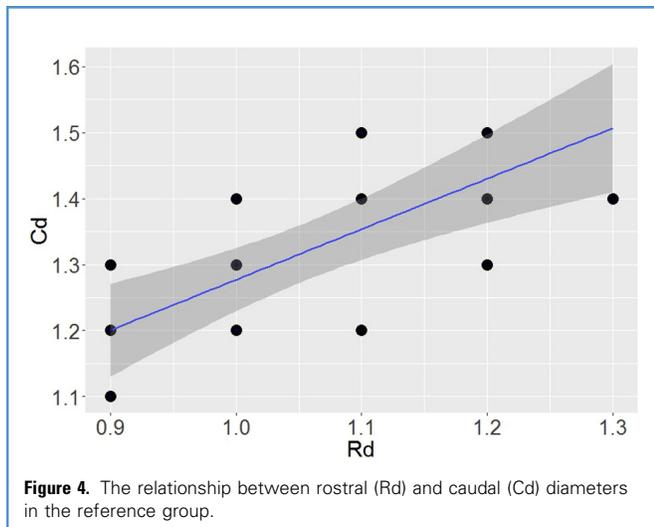
### Surgery and Outcome

In all patients microsurgical cyst removal was performed in a sitting position through the infratentorial supracerebellar approach. Care was taken not to injure the bridging veins between the cerebellum and the tentorium and the precentral cerebellar vein. All patients underwent complete cyst resection confirmed by postoperative MRI scans. Pathologic diagnosis confirmed simple pineal cysts in all cases. The mean clinical follow-up period was 4.7 years (ranging 1–15 years). In 25 patients (82%) we observed clinical improvement after surgery in a follow-up period. Among those with improvement, 10 patients (40%) experienced total relief and 15 of them (60%) had marked headache relief with little to no HIT-6 impact score. In 5 patients headache remained persistent with substantial ( $n = 3$ ) and severe ( $n = 2$ ) HIT-6 impact score. Dizziness and syncope resolved in all cases.

The postoperative mortality was null. One patient suffered from air embolism during surgery, which wasn't hemodynamically significant and eventually had no impact on the postoperative course. Another patient had postoperative incisional cerebrospinal fluid leak, which resulted in nosocomial meningitis. However, this patient was successfully treated and discharged from the hospital without additional neurologic deficit. Five patients (17%) in the postoperative period had transient upward gaze palsy and disconjugate eye movements, which resulted in transient diplopia.

### MRI Findings

In a group of patients who underwent surgical treatment the mean anterior-posterior cyst diameter was  $19 \pm 3$  mm (ranging 9–29), craniocaudal diameter was  $17 \pm 3$  mm (ranging 4–22), and transverse diameter was  $14 \pm 3$  mm (ranging 8–20). The mean cyst volume was  $18 \pm 8$  mm<sup>3</sup> (ranging 2–40). Evan's ratio appeared to be  $< 0.3$  (average  $0.25 \pm 0.02$ , ranging 0.22–0.28) in



all cases. Cyst diameters in all 3 dimensions and cyst volume weren't significantly different in groups with clinical improvement and without it ( $P = 0.5194$ ,  $P = 0.4999$ ,  $P = 0.634$ ,  $P = 0.7384$ ). However, the anterior-posterior cyst diameter showed a strong correlation with the rostral diameter of the CAQ ( $\rho = -0.4579141$ ,  $P = 0.0109$ ).

In a group of patients who did not undergo surgical treatment, the mean anterior-posterior cyst diameter was  $15 \pm 4$  mm (ranging 7–24), the craniocaudal diameter was  $9 \pm 3$  mm (ranging 4–14), and the transverse diameter was  $14 \pm 3$  mm (ranging 7–13). Surgically removed PCs appeared to be larger in anterior-posterior and craniocaudal dimensions ( $P = 0.006$ ,  $P$  value = 0.001) than nonoperated PCs.

The average (avg.) values for the rostral and caudal CAQ diameters in the reference group were  $1.1 \pm 0.2$  mm and  $1.3 \pm 0.1$  mm, respectively. The rostral and caudal diameters showed variability but were strongly correlated ( $\rho = 0.74$ ,  $P = 0.00002$ , **Figure 4**). The Rd/Cd ratio in the reference group ranged from 0.69–1.4 (avg.  $0.83 \pm 0.14$ ). The same measurements were made in the remaining 2 groups and are presented in **Table 1**.

The comparison of obtained morphometric data was conducted among all 3 groups. There was no difference in caudal diameter of CAQ in a group of patients who underwent surgical removal of PCs ( $n = 30$ ) compared with the reference group ( $n = 25$ ) ( $P = 0.07$ ) and nonoperated cysts ( $n = 22$ ) ( $P = 0.325$ ). Comparison of the Cd within the reference group and patients followed conservatively also showed no difference ( $P = 0.408$ ). The CAQ diameters on the

preoperative rostral sections and Rd/Cd ratio in patients with operated PCs were further compared with the reference group, revealing a significant statistical difference: patients with PCs had a narrower rostral part of the CAQ ( $P = 0.0000017$ ) and their Rd/Cd ratios were significantly lower ( $P = 0.0000003$ ). We also found that either the preoperative rostral section of the CAQ or the Rd/Cd ratio was narrower ( $P = 0.000018$ ) and lower ( $P = 0.00001$ ) in the surgically treated group versus nonoperated PCs. However, the Rd and Rd/Cd ratio between healthy individuals and patients who didn't undergo surgery didn't differ ( $P = 0.2053$ ).

To assess the relation between the clinical outcome and changes in CAQ morphometry in postoperative period, Rd, Rd/Cd ratio, and the postoperative value increase were compared (**Table 2**).

The preoperative Rd/Cd ratio was found to be lower ( $P = 0.004391$ ), and the postoperative increase of Rd/Cd ratio was significantly higher ( $P = 0.0005077$ ) in patients with clinical improvements (**Figure 5**). The preoperative ( $0.79 \pm 0.24$ ) Rd/Cd ratios didn't differ significantly from postoperative ( $0.82 \pm 0.19$ ) in the group of patients with no clinical improvement ( $P = 1$ ) and resembled that of healthy individuals ( $0.911$ ) (**Figure 6**).

The preoperative rostral CAQ diameter appeared to be significantly narrower in patients who recovered from headache (average  $0.7$  mm  $\pm$   $0.2$  mm, range 0.3–1.1) versus those who did not (average  $1.1$  mm  $\pm$   $0.2$  mm, range 0.9–1.5) ( $P$  value = 0.0011045). The postoperative increase of Rd was also significantly higher in the group of patients with clinical improvements ( $P = 0.0011912$ ). Comparing the preoperative morphometrics of the CAQ in patients with different clinical outcome with the reference group, the statistical difference was found only in the group of patients who had clinical improvements (**Figure 7**).

Either the preoperative Rd or the Rd/Cd ratio was narrower ( $P = 0.0000005$ ) and lower ( $P = 0.0000003$ ) in patients who recovered from headache versus patients with nonoperated PCs. Conducting the same comparison values in patients without clinical improvement and PCs followed conservatively, no statistical difference was observed ( $P = 0.07$ ,  $P = 0.975$ ).

The diagnostic and prognostic values of the Rd and Rd/Cd ratio can be simultaneously explored in **Figure 8**. In our cohort, all patients with preoperative Rd not exceeding 0.8 mm benefited from surgery. We found that patients with clinical improvements had a significantly lower preoperative Rd/Cd ratio ( $P = 0.004391$ ) than patients with no clinical improvements. A positive outcome was observed in all 11 (40.7%) patients with a preoperative Rd/Cd ratio  $\leq 0.56$ . Patients with preoperative Rd/Cd  $\geq 0.79$  showed no clinical improvement ( $n = 3$ ). Both positive ( $n = 14$ ) and negative ( $n = 2$ ) outcomes could be observed in patients with preoperative Rd/Cd ratios between

**Table 1.** Cerebral Aqueduct Morphometric Data in 3 Comparison Groups

Parameter	Reference Group (n = 25)	Surgically Treated Group (n = 30)	Group of Pineal Cysts Without Surgery (n = 22)
Rostral diameter (Rd), mm	$1.06 \pm 0.126$	$0.75 \pm 0.26$	$1 \pm 0.2$
Caudal diameter (Cd), mm	$1.3 \pm 0.1$	$1.43 \pm 0.22$	$1.4 \pm 0.2$
Rd/Cd ratio	$0.83 \pm 0.13$	$0.54 \pm 0.20$	$0.7 \pm 0.1$

**Table 2.** Comparison of Cerebral Aqueduct Morphometry in Patients with Pineal Cysts in Relation to Different Clinical Outcome After Surgery

Parameter	Clinical Improvement (n = 25)	No Clinical Improvement (n = 5)	P Value
Preoperative Rd	0.7 ± 0.2 (0.3–1.1)	1.1 ± 0.2 (0.9–1.1)	0.001
Preoperative Rd/Cd	0.49 ± 0.14 (0.2–0.78)	0.79 ± 0.24 (0.56–1.15)	0.004
Postoperative Rd	1.25 ± 0.19 (0.9–1.7)	1.18 ± 0.27 (0.9–1.5)	0.8
Postoperative Rd/Cd	0.91 ± 0.19 (0.69–1.46)	0.82 ± 0.19 (0.56–1.07)	0.54
Postoperative Rd increase*	0.57 ± 0.25 (0–1)	0.06 ± 0.09 (0.9–1.1)	0.001
Postoperative Rd/Cd increase*	0.42 ± 0.23 (0–0.99)	0.03 ± 0.09 (–0.08–0.14)	0.0005

\*Postoperative increase is calculated as the difference between postoperative and preoperative measurements in each patient.

0.56 and 0.79. The clinical improvement after surgery was observed in those patients whose Rd/Cd ratio increased by 0.19 or more after operation depending on preoperative Rd.

Figure 9 presents the comparison of the preoperative Rd/Cd ratio among patients with different clinical outcome, reference group, and patients with nonoperated PCs. A statistical significance was certain for patients with clinical improvement.

## DISCUSSION

Improvements of diagnostic methods increased the prevalence of accidental pineal cyst findings.<sup>3,4,9,11</sup> Despite this fact, the management of these benign lesions is the subject of debate and the indications for surgery are still evolving.

Often the most common and only clinical manifestation of pineal cysts is headache. According to the literature, headache was described in 81% of surgical cases.<sup>20</sup> Decision making for surgical intervention in patients with PCs where headache is the only symptom could be complicated and may expose patients to the risk of surgery. Furthermore, headache is also common in the general population. Whereas headaches and pineal cysts are both highly encountered in clinical practice, their coexistence is more likely to be incidental. Currently, it is not established

whether surgical removal of nonhydrocephalic PCs leads to headache relief or not. According to the world survey, most surgeons would not consider surgery as a first-line treatment in patients with PCs whose symptoms are only headache.<sup>11</sup>

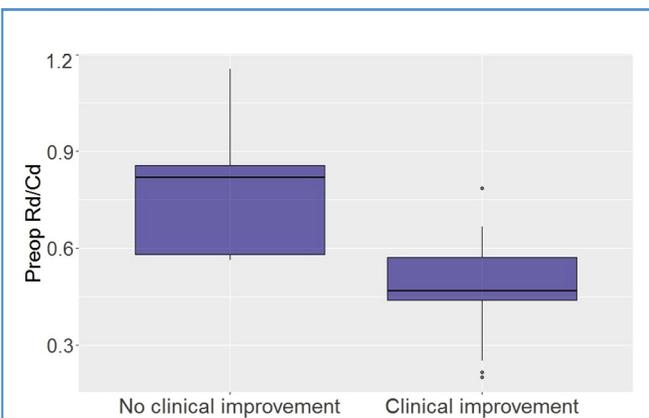
Moreover, defining which patients should be offered neurosurgical intervention is especially challenging as the role of PC as a trigger of headache in the absence of hydrocephalus is still unclear.

However, various factors might be responsible for headaches. The authors had hypothesized that a possible explanation of PC-related headache could be linked to melatonin-level disturbances,<sup>21–23</sup> obstacles of the CSF flow through the cerebral aqueduct, which may lead to obstructive hydrocephalus with elevated intracranial pressure and pineal apoplexy.<sup>24</sup> One of the latest hypotheses regarding symptomatic nonhydrocephalic PCs is the crowding pineal recess theory.<sup>15,17</sup> The authors believe that the PC-associated compression on the deep-seated veins increases back pressure, which might increase the interstitial water content and cause extracellular edema. Several authors had also reported that positional headaches, paroxysmal syncope, and even death can be associated with intermittent obstruction of CSF pathways caused by PCs.<sup>14,15,25,26</sup>

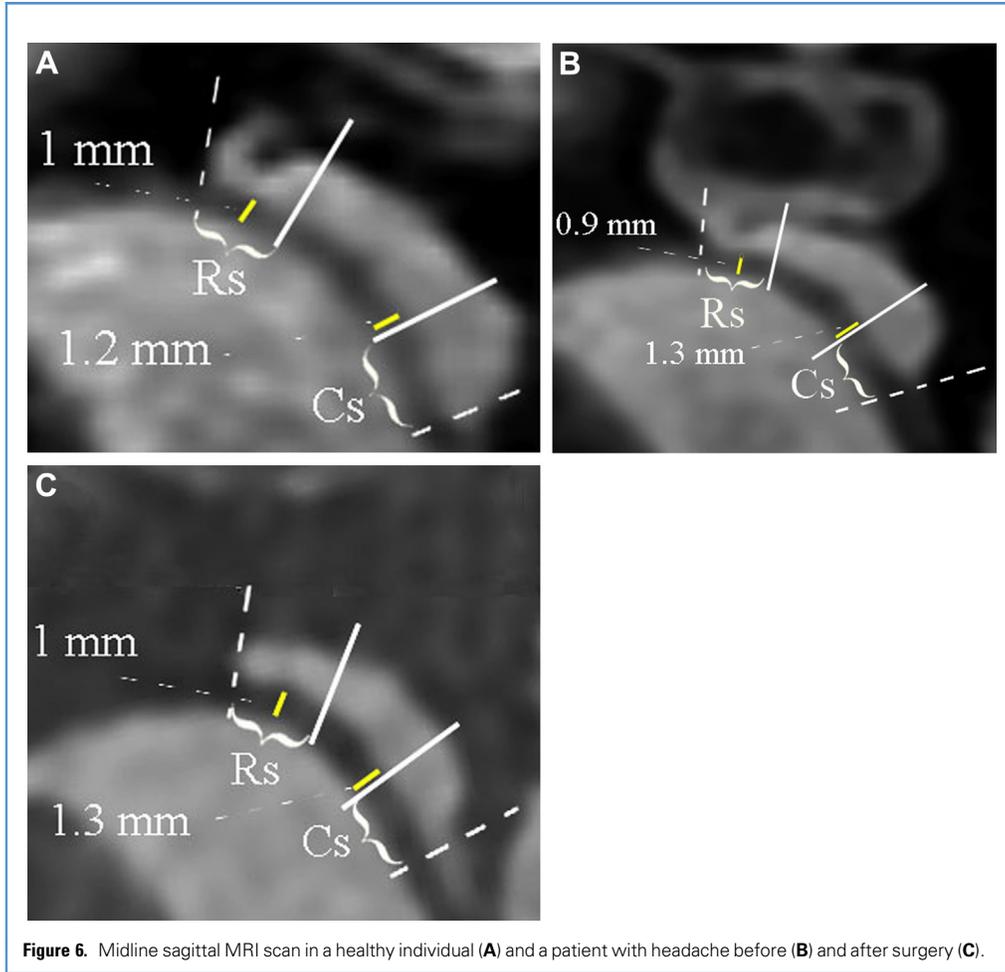
Nevertheless, indications for surgical management of PC have expanded over the past 2 decades. Seventy-eight histologically confirmed cases had been reported from 1914–2000, while after the year 2000 this number doubled and reached 168.<sup>20</sup> Recent publications have shown that surgery can be acceptable in “borderline” cases after a thorough workup.<sup>11,14,17,27</sup> All these studies have demonstrated a resolution of headaches in 90%–100% of patients after surgery. Considering the information stated earlier, patients with symptomatic PCs in the absence of hydrocephalus and without Parinaud syndrome can also benefit from surgery.

### Cerebral Aqueduct Stenosis in Patients with Headache Harboring Pineal Cysts

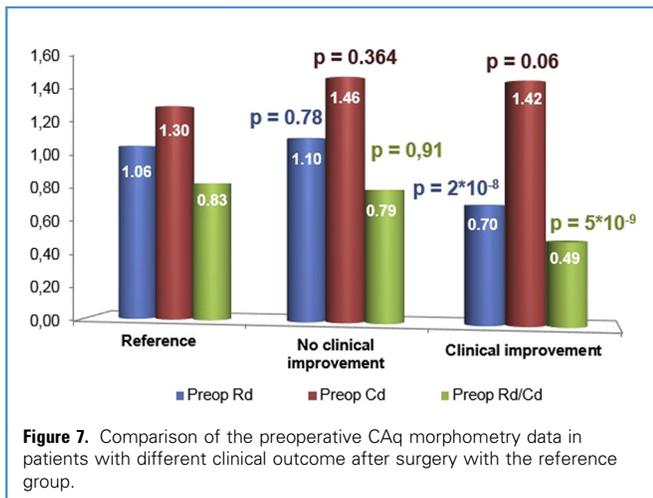
Cerebral aqueduct stenosis and cyst size are commonly encountered factors taken into consideration in the management of symptomatic nonhydrocephalic PCs.<sup>6,7,11,14–17</sup> Considering that stenosis of the rostral part of the CAq can be observed in patients with headache harboring PC in the absence of hydrocephalus, we



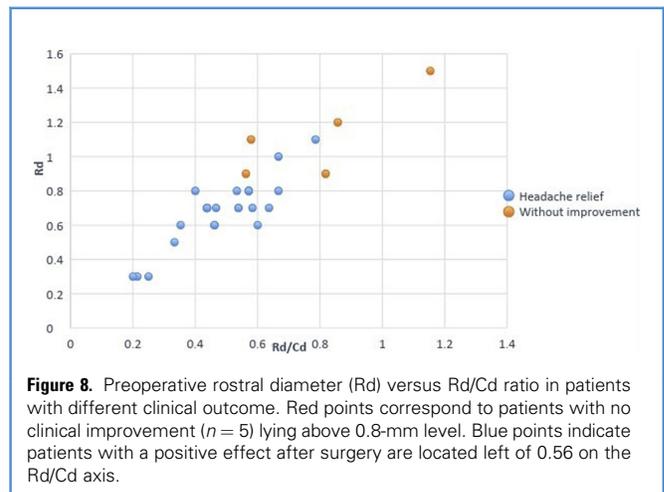
**Figure 5.** The preoperative Rd/Cd ratio in patients with and without clinical improvement.



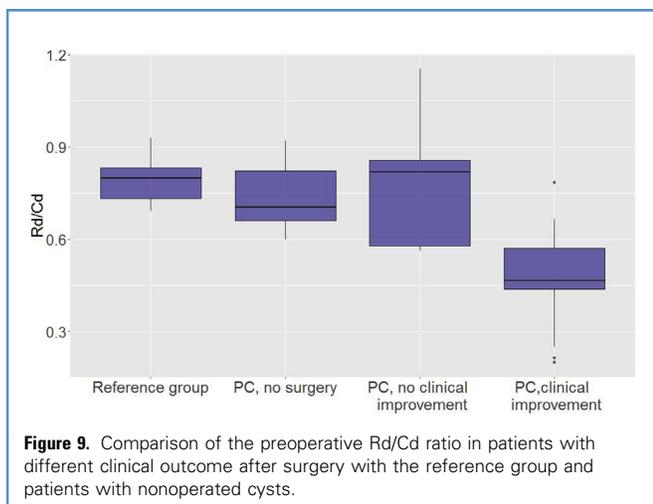
**Figure 6.** Midline sagittal MRI scan in a healthy individual (A) and a patient with headache before (B) and after surgery (C).



**Figure 7.** Comparison of the preoperative CAq morphometry data in patients with different clinical outcome after surgery with the reference group.



**Figure 8.** Preoperative rostral diameter (Rd) versus Rd/Cd ratio in patients with different clinical outcome. Red points correspond to patients with no clinical improvement ( $n = 5$ ) lying above 0.8-mm level. Blue points indicate patients with a positive effect after surgery are located left of 0.56 on the Rd/Cd axis.



decided to evaluate the changes in the CAq morphometrics after surgery and inspect their relationship with the dynamics of clinical symptoms.

Variations in normal CAq morphometry have been previously described by Matys et al.<sup>19</sup> The authors reported on cerebral aqueduct morphometrics based on 3-T MRI. Their technique of precise measurements provided physicians with detailed information on the normal aqueduct anatomy. It was shown that the normal CAq diameter on the rostral and caudal sections of the aqueduct in the population averaged  $1.1 \pm 0.3$  mm and  $1.4 \pm 0.3$  mm, respectively, and did not depend on gender.

The rostral and caudal diameters of the cerebral aqueduct and their ratio were hypothesized to have diagnostic and prognostic values in patients harboring PC in the absence of secondary hydrocephalus. To prove this hypothesis we started with evaluating the previously mentioned morphometrics of the CAq and their ratio in patients without brain pathology (reference group).

Our research showed that the data obtained from healthy individuals were similar to that described by Matys et al.<sup>19</sup> (Figure 4). Comparing the morphometrics of CAq between our groups, we found that only the rostral diameter was affected by PC compression in patients with headache. Hence a different degree of rostral CAq stenosis can be observed in patients with pineal cysts. On the basis of the results of the morphometry study, we found that asymptomatic patients followed conservatively had similar CAq configuration to patients without clinical improvement and healthy individuals.

The obtained data indicated that the geometry of the CAq undergoes certain changes after the operation, specifically in its rostral section. The preoperative rostral diameter was narrower, and the Rd/Cd ratio was lower in patients who had headache relief after surgery 92% ( $n = 23$ ). However, in our series the rostral diameter appeared to have a better prognostic value than Rd/Cd ratio. In 2 patients with clinical improvement the rostral diameter exceeded 0.8 mm (1 mm and 1.1 mm). The possible explanation of the positive effect from surgery in these patients is not obvious,

and 1 reasons could be a measurement inaccuracy. In our series all 11 (44%) patients with preoperative Rd/Cd ratio  $\leq 0.56$  benefited from surgery. Thus the prognostic value of the preoperative Rd/Cd ratio in our study was lower than the predictive power of rostral CAq diameter. On the other hand, the absolute diameter value shouldn't be overestimated as it can vary on different MRI sequences in 1 patient. In such cases the Rd/Cd ratio is more reliable for predictive calculations because it reflects variation in both diameters simultaneously.

Five patients did not experience headache relief after surgery. A possible reason for the lack of clinical improvement in these patients could be related to improper selection for surgery. It is worth noting that there was no statistically significant difference in Rd/Cd ratios in the preoperative and postoperative periods in the group of patients with PC who did not experience any clinical improvement after surgery ( $P = 1$ ). Also, we found that there was no significant difference ( $P = 0.911$ ) between Rd/Cd ratio in reference group and preoperative Rd/Cd ratio in patients without clinical improvements. Our observation may indicate that aqueduct configuration in patients with clinical improvement after PC removal undergoes obvious changes, while preoperative CAq morphometry in patients with no clinical improvement resembles that found in healthy individuals.

### Limitations

The main limitation of our research is that it is a retrospective study with an insufficient level of evidence. The present cohort included 30 patients, 5 of them without clinical improvement after surgery, which was a rather low number for the powerful statistical evaluation. However, considering that symptomatic PCs without hydrocephalus are rare, the planning of a multicenter study is reasonable. Another weakness is the method for CAq geometry assessment. More sophisticated protocols aimed at providing even higher resolution and isometric voxels for measuring aqueductal dimensions should be added for further studies. We do not propose our method of CAq morphometry evaluation as the primary one in decision making about the symptomatic nonhydrocephalic PC treatment, but rather as an additional tool.

Despite these limitations, our study provides the most convincing evidence yet presented that CAq stenosis can be associated with disabling headache in patients with PC in the absence of ventriculomegaly.

### CONCLUSION

This is the first study that shows changes in the cerebral aqueduct morphometry after PC surgical removal. We found a statistically significant relationship between the changes in the CAq morphometrics after operation and the clinical outcome. For symptomatic pineal cysts without hydrocephalus, a surgical resection can lead to headache relief or decrease its frequency and severity. However, the decision to offer surgery shouldn't be based on CAq morphometry only but instead on a combination of clinical symptoms, thorough preoperative examination, and the patient's subjective perception of disabling headache and its impact on everyday life.

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