**Headache outcomes after surgery for pineal cyst without hydrocephalus: A systematic review**

Camille K. Milton, Panayiotis E. Pelargos, Ian F. Dunn

Department of Neurosurgery, University of Oklahoma Health Sciences Center, Oklahoma City, United States.

E-mail: Camille K. Milton - camille-milton@ouhsc.edu; Panayiotis E. Pelargos - panayiotis-pelargos@ouhsc.edu; *Ian F. Dunn - ian-dunn@ouhsc.edu

*Corresponding author:

Ian F. Dunn,
Department of Neurosurgery,
University of Oklahoma Health Sciences Center, Oklahoma City, United States.
ian-dunn@ouhsc.edu

Received : 16 August 2020
Accepted : 16 October 2020
Published : 11 November 2020

DOI:
10.25259/SNI_541_2020

Quick Response Code:

**ABSTRACT**

**Background:** Pineal cysts are common entities, with a reported prevalence between 10 and 54%. Management of pineal cysts has historically been expectant, with surgical treatment of these lesions usually reserved for patients with a symptomatic presentation secondary to mass effect. The appropriate management of pineal cysts in patients presenting with headache in the absence of hydrocephalus – often the most common clinical scenario – has been more ambiguous. Here, we report the results of a comprehensive systematic review of headache outcomes for surgically treated, non-hydrocephalic pineal cyst patients without signs of increased intracranial pressure (ICP).

**Methods:** Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines were followed to construct a systematic review. A comprehensive search of PubMed, Embase, Scopus, and Web of Science databases was conducted from through June 2020. Relevant English-language articles were identified using the search terms “pineal cyst” and “headache.” The following eligibility criteria were applied: the inclusion of at least one surgically-treated, non-hydrocephalic pineal cyst patient presenting with headache in the absence of hemorrhage or signs and symptoms of increased ICP. Patient demographics and post-operative headache outcomes for the included studies were extracted and summarized.

**Results:** A total of 24 pineal cyst cases meeting our selection criteria were identified across 11 included studies. Postoperative improvement or resolution of headaches was reported for 23/24 patients. Our systematic review of the literature demonstrates that non-hydrocephalic patients with pineal cysts have a high rate of headache improvement following surgical intervention.

**Conclusion:** The results indicate a need for further investigation of the link between headache and pineal cysts in the non-hydrocephalic patient.

**Keywords:** Headache, Hydrocephalus, Pineal cyst, Surgery

**INTRODUCTION**

Pineal cysts are common, often incidental, findings with an estimated prevalence between 10 and 54% in the general population.[23] The natural history of pineal cysts is characterized by a higher prevalence in younger female patients and lesion stability on radiographic follow-up.[1] Surgical treatment of pineal cysts has historically been reserved for patients with a symptomatic presentation secondary to mass effect manifesting with hydrocephalus or upgaze palsy. Despite the fact that headache without hydrocephalus is much more common than the classical Parinaud
syndrome presentation, the ideal management of these patients has not been established. Nevertheless, it remains an important question due to the quandary of effective headache control in this patient population. A causal relationship between headache and pineal cysts without hydrocephalus has been proposed by a small number of studies with results suggesting that pineal cysts may be mislabeled as incidental in a subset of headache patients.\(^5\)\(^,\)\(^9\) Nevertheless, there are a lack of data assessing headache outcomes for nonhydrocephalic pineal cyst patients. Here, we report the results of a systematic review of headache improvement for all published surgically treated, nonhydrocephalic pineal cyst patients, with the primary outcome measure the reported postoperative headache improvement rate in this patient population.

**MATERIALS AND METHODS**

Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were followed to construct a systematic review of all previously reported surgically treated pineal cyst patients presenting with headache without hydrocephalus or upgaze palsy.\(^1\)\(^,\)\(^2\)\(^,\)\(^3\)\(^,\)\(^4\)\(^,\)\(^5\)\(^,\)\(^6\)\(^,\)\(^7\)\(^,\)\(^8\)\(^,\)\(^9\) Methods of analysis and inclusion criteria were specified and documented in a protocol before initiation of the search. A search of the PubMed, Embase, Scopus, and Web of Science databases was conducted in June 2020. Relevant articles were identified using the search terms “pineal cyst” and “headache.” Searches were restricted to the English language. No restrictions on study design, publication date, or publication status were imposed. Titles and abstracts for the resultant 319 records were screened for relevance. One hundred and ninety nine records evaluating pathology other than pineal cysts were discarded. Full-text manuscripts were reviewed for the remaining 120 records. Conference abstracts, review articles, book chapters, and autopsy cases were excluded from the study. The following eligibility criteria were applied to the remaining studies: the inclusion of at least one surgically treated, nonhydrocephalic pineal cyst patient presenting with headache. Cases exhibiting intracystic hemorrhage were discarded. Records that included subjects whose headaches were accompanied by symptoms concerning for increased intracranial pressure (ICP) such as nausea, vomiting, lethargy, fatigue, vertigo, tinnitus, oculomotor dysfunction, blurred vision, diplopia, papilledema, syncope, seizure, or focal neurologic deficit, were excluded from the study. Finally, records that did not specify the number of patients presenting with headache as an individual symptom or those that failed to provide postoperative headache outcomes were excluded from the study.

Patient demographics and postoperative headache outcomes for the included studies were extracted and reviewed and agreed on by two reviewers. The primary outcome of our analysis was the postoperative headache improvement rate for surgically treated, nonhydrocephalic pineal cyst patients presenting with headache alone. Ultimately, 11 studies were incorporated into our systematic review. A flow chart depicting our study selection process is shown in [Figure 1].\(^5\)\(^,\)\(^7\)\(^,\)\(^8\)\(^,\)\(^9\)\(^,\)\(^10\)\(^,\)\(^11\)\(^,\)\(^14\)\(^,\)\(^16\)\(^-\)\(^19\)\(^,\)\(^22\)

**RESULTS**

Twenty-four pineal cyst patients were identified across the 11 included studies. Among the analyzed articles, three were single-subject case reports, three incorporated 2–10 total subjects, and five incorporated more than ten total subjects [Table 1]. Mean patient age was 27.0 years and 23/24 subjects (96%) were female. Preoperative headache symptom duration was 27.3 months on average. Mean length of follow-up for studies in which individual subject follow-up was reported was 13.9 months. Postoperative improvement or resolution of headaches was reported for 23/24 patients (96%). The average maximum dimension of pineal cysts was

| Author date | Journal | Study type | Total reported subjects | Subjects meeting inclusion criteria |
|-------------|---------|------------|-------------------------|-----------------------------------|
| Klein and Rubinstein, 1989 | J Neurol Neurosurg Psychiatry | Retrospective series | 7 | 1 |
| Fleeg et al., 1994 | AJNR Am J Neuroradiol | Retrospective series | 19 | 5 |
| Michielsen et al., 2002 | Acta Neurochir (Wien) | Retrospective series | 7 | 1 |
| Mandera et al., 2003 | Childs Nerv Syst | Retrospective series | 24 | 1 |
| Stevens et al., 2007 | Child Neurol | Case report | 1 | 1 |
| Kahilogullari et al., 2013 | Childs Nerv Syst | Case report | 1 | 1 |
| Meyers et al., 2013 | Acta Paediatr | Case report | 1 | 1 |
| Majovsky et al., 2017 | World Neurosurg | Prospective | 110 | 3 |
| Majovsky et al., 2017 | J Clin Neurosci | Prospective | 7 | 1 |
| El Damaty et al., 2019 | World Neurosurg | Retrospective series | 43 | 5 |
| Kozierski et al., 2019 | Br J Neurosurg | Retrospective series | 28 | 4 |

Total 248 24
1.5 cm. Pineal cysts were resected using a supracerebellar infratentorial approach in 21/24 cases, and an occipital transtentorial approach in 1 case. Operative approach was not reported for two cases. Two operative complications were reported: a hematoma of the posterior third ventricle that resolved spontaneously and a small venous cerebellar infarction.

Headache outcomes were not stratified to separate individuals presenting with headache alone in one study. In this case, a personal correspondence with the author clarified the outcomes for the included subset of patients. Methods of measuring postoperative improvement varied. Brief, qualitative statements such as “the patient’s headaches were improved/resolved at follow-up” represented the most common method of reporting symptomatic outcomes across the included studies. Only three of the studies reported the use of standardized symptom scoring systems such as the Chicago Chiari Outcome Scale or visual analog scale. The results of our review of the literature including patient demographics, clinical characteristics, and postoperative headache outcomes are summarized in Table 2.

**DISCUSSION**

Symptomatic pineal cysts have classically been defined as producing one of the three syndromes: (1) paroxysmal
Table 2: Patient demographics, clinical characteristics, and postoperative headache outcomes for published cases of pineal cysts presenting with headache in the absence of hydrocephalus or symptoms of increased intracranial pressure.

| Publication | Patient demographics | Clinical characteristics | Postoperative outcomes |
|-------------|----------------------|--------------------------|------------------------|
| Klein and Rubinstein, 1989 | F | 22 | N | 12 | Headache | NR | Immediate post-operative follow-up; Lost to long-term follow-up | None | “After operation the headache cleared” | Yes |
| Fleeger et al., 1994 | M | 16 | 1.0 | NR | Headache | Supracerebellar infratentorial | 3–5 months | None | “Asymptomatic” | Yes |
| | F | 39 | 1.0 | NR | Headache | Supracerebellar infratentorial | 3–5 months | None | “Asymptomatic” | Yes |
| | F | 36 | 1.8 | NR | Headache | Supracerebellar infratentorial | 3–5 months | None | “Asymptomatic” | Yes |
| | F | 46 | 1.8 | NR | Headache | Supracerebellar infratentorial | 3–5 months | None | “Asymptomatic” | Yes |
| Michielsen et al., 2002 | F | 27 | 2.0 | 48 | Headache | Supracerebellar infratentorial | 12 months | None | “Patient maintained their headache” | No |
| Mandera et al., 2003 | F | 15 | <2.0 | NR | progressive headache | Supracerebellar infratentorial | 31 months* | None | “Free of symptoms” | Yes |
| Stevens et al., 2007 | F | 13 | 1.8 | 14 | Headache | Supracerebellar infratentorial | 1 month | None | “Headache free” | Yes |
| Kahilogullari et al., 2013 | F | 13 | 1.6 | 36 | progressive headache | Occipital transtentorial | 6 months | None | “headache free” | Yes |
| Meyer et al., 2013 | F | 14 | NR | 7 | chronic intermittent headache | NR | NR | None | “After surgery headache symptoms resolved” | Yes |
| Majovsky et al., 2017 | F | 50 | 1.3 | 48 | Worsening tension headache | Supracerebellar infratentorial | NR | None | “Headache improved” | Yes |
| Publication         | Patient demographics | Clinical characteristics | Postoperative outcomes |
|---------------------|----------------------|--------------------------|------------------------|
|                     | Gender | Age (years) | Largest tumor dimension (cm) | Symptom duration (months) | Clinical presentation | Approach to resection | Length of post-operative follow-up | Operative complication | Headache outcome description | Headaches improved or resolved? |
| Majovsky et al., 2017 | F     | 22         | 1.4 | NR | "Intractable headache" | Supracerebellar infratentorial | NR | None | "Substantial improvement in presenting symptoms" | Yes |
| El Damaty et al., 2019 | F     | 33         | 1.1 | NR | Headache | Supracerebellar infratentorial | 3.74 years* | None | "No complaints" | Yes |
|                     | F     | 20         | 1.1 | NR | Headache | Supracerebellar infratentorial | 3.74 years* | None | "No complaints" | Yes |
|                     | F     | 27         | 1.9 | NR | Headache | Supracerebellar infratentorial | 3.74 years* | None | "Headache improved" | Yes |
|                     | F     | 26         | 1.9 | NR | Headache | Supracerebellar infratentorial | 3.74 years* | None | "No complaints" | Yes |
|                     | F     | 7          | 1.1 | NR | Headache | Supracerebellar infratentorial | 3.74 years* | None | "Headache improved markedly" | Yes |
| Kozierski et al., 2019 | F     | 35         | 1.9 | 36 | Headache | Supracerebellar infratentorial | 12 months | None | "Free of preoperative symptoms" | Yes |
|                     | F     | 42         | 1.7 | 48 | Headache | Supracerebellar infratentorial | 13 months | None | "Free of preoperative symptoms" | Yes |
|                     | M     | 21         | 1.3 | 24 | Headache | Supracerebellar infratentorial | 14 months | None | "Free of preoperative symptoms" | Yes |
|                     | F     | 42         | 1.5 | 6 | Headache | Supracerebellar infratentorial | 15 months | None | "Free of preoperative symptoms" | Yes |

NR: Not reported. * Mean duration of follow-up reported for larger cohort
headache with gaze paresis, (2) chronic headache, gaze paresis, papilledema, and hydrocephalus, or (3) pineal apoplexy with acute hydrocephalus.\textsuperscript{12-14} Pineal cysts detected in the absence of these contexts have typically been considered asymptomatic in the neurosurgical community. However, the assumption that a pineal cyst is always an incidental finding in a patient with primary headache and no signs or symptoms of mass effect has been challenged in recent years.\textsuperscript{6,20} A case-control study of 51 non-hydrocephalic pineal cyst patients supported a causal relationship between headaches and pineal cysts that was independent of cyst size. In this particular study, headache frequency in patients with pineal cysts was twice that of age- and sex-matched controls.\textsuperscript{14}

Popular explanations for a causal link between pineal cysts and headaches in non-hydrocephalic patients include altered melatonin secretion and intermittent aqueduct obstruction.\textsuperscript{2,17,20,21,24} Pulsatile ICP appears to be increased in individuals with symptomatic non-hydrocephalic pineal cysts as compared to individuals with chronic daily headache alone.\textsuperscript{4} Pulsatile ICP was calculated in this study as the product of the mean ICP wave amplitude (MWA), the mean ICP wave rise time (MWRT), and a MWRT coefficient.\textsuperscript{4} Furthermore, symptom severity in non-hydrocephalic pineal cyst patients is associated with MRI biomarkers of central venous hypertension including tectum-splenium-cyst ratio and indices of thalamic and periventricular edema.\textsuperscript{3}

Nevertheless, the surgical management of pineal cysts remains controversial and continues to be an important question given the prevalence of headache and pineal cyst. A worldwide online survey of 110 neurosurgeons demonstrated that hydrocephalus (90%), Parinaud's syndrome (80%), and cyst growth (68%) were the most commonly identified indications for surgical resection of pineal cysts. Only 15% of the respondents reported that they occasionally operate on patients with non-specific symptoms such as headache.\textsuperscript{13} A 2017 review on the surgical management of pineal cysts found a relatively high rate of symptom improvement (42.9–100%) in the six reviewed clinical series addressing clinical outcome, despite the fact that most patients presented with non-specific symptoms including headache. The authors acknowledged the limited availability of data on the surgical treatment of pineal cysts and conclude that a registry of symptomatic pineal cyst patients might assist neurosurgeons in standardizing the criteria used to identify surgical candidates.\textsuperscript{13}

Our comprehensive review of the literature suggests that non-hydrocephalic patients with pineal cysts have a high rate of headache improvement after surgical intervention. However, we acknowledge some limitations to our study. First, the majority of articles incorporated in our analysis are small, non-comparative, and retrospective studies. In the absence of a blinded trial comparing headache outcomes in surgically treated versus nonsurgically treated patients, we cannot discount the potential for significant selection and reporting bias.\textsuperscript{23} Second, few of the included studies reported quantitative assessments of headaches either preoperatively or at postoperative follow-up. Descriptive statements such as “headaches were resolved,” or “headaches were improved” were commonly encountered. Third, detailed qualitative descriptions of headaches were lacking for almost all included studies.

Despite these limitations, our results indicate the need for further investigation of the link between headache and pineal cysts in the nonhydrocephalic patient. We propose the development of a consensus-derived quantitative measure for grading headache severity and assessing surgical candidacy in these patients.

Declaration of patient consent

Patient's consent not required as there are no patients in this study.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Al-Holou WN, Terman SW, Kilburg C, Garton HJ, Muraszko KM, Chandler WF, \textit{et al}. Prevalence and natural history of pineal cysts in adults. J Neurosurg 2011;115:1106-14.
2. Berhouma M, Ni H, Delabar V, Tahhan N, Salem SM, Mottolese C, \textit{et al}. Update on the management of pineal cysts: Case series and a review of the literature. Neurochirurgie 2015;61:201-7.
3. Eide PK, Pripp AH, Ringstad GA. Magnetic resonance imaging biomarkers indicate a central venous hypertension syndrome in patients with symptomatic pineal cysts. J Neurol Sci 2016;363:207-16.
4. Eide PK, Ringstad G. Increased pulsatile intracranial pressure in patients with symptomatic pineal cysts and magnetic resonance imaging biomarkers indicative of central venous hypertension. J Neurol Sci 2016;367:247-55.
5. El Damaty A, Fleck S, Matthes M, Baldauf J, Schroeder HW. Pineal cyst without hydrocephalus: Clinical presentation and postoperative clinical course after infratentorial supracerebellar resection. World Neurosurg 2019;129:e530-7.
6. Evans RW, Peres MF. Headaches and pineal cysts. Headache 2010;50:666-8.
7. Fleeye MA, Miller GM, Fletcher GP, Pain JS, Scheithauer BW. Benign glial cysts of the pineal gland: Unusual imaging
8. Kahilogullari G, Massimi L, di Rocco C. Pineal cysts in children: Case-based update. Childs Nerv Syst 2013;29:753-60.

9. Kalani MY, Wilson DA, Koechlin NO, Abuhussain HJ, Dlouhy BJ, Gunawardena MP, et al. Pineal cyst resection in the absence of ventriculomegaly or Parinaud’s syndrome: Clinical outcomes and implications for patient selection. J Neurosurg 2015;123:352-6.

10. Klein P, Rubinstein LJ. Benign symptomatic glial cysts of the pineal gland: A report of seven cases and review of the literature. J Neurol Neurosurg Psychiatry 1989;52:991-5.

11. Koziarski A, Podgorski A, Zielinski GM. Surgical treatment of pineal cysts in non-hydrocephalic and neurologically intact patients: Selection of surgical candidates and clinical outcome. Br J Neurosurg 2019;33:37-42.

12. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gotzsche PC, Ioannidis JP, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: Explanation and elaboration. BMJ 2009;339:b2700.

13. Majovsky M, Netuka D, Benes V. Clinical management of pineal cysts: A worldwide online survey. Acta Neurochir (Wien) 2016;158:663-9.

14. Majovsky M, Netuka D, Benes V. Conservative and surgical treatment of patients with pineal cysts: Prospective case series of 110 patients. World Neurosurg 2017;105:199-205.

15. Majovsky M, Netuka D, Benes V. Is surgery for pineal cysts safe and effective? Short review. Neurosurg Rev 2018;41:119-24.

16. Majovsky M, Rezacova L, Sumova A, Pospisilova L, Netuka D, Bradac O, et al. Melatonin and cortisol secretion profile in patients with pineal cyst before and after pineal cyst resection. J Clin Neurosci 2017;39:155-63.

17. Mandera M, Marcol W, Bierzyńska-Macyszyn G, Kluczewska E. Pineal cysts in childhood. Childs Nerv Syst 2003;19:750-5.

18. Meyer S, Oberkircher N, Boing A, Larsen A, Eymann R, Kutschke G. Disturbance in melatonin metabolism as a causative factor for recurrent headaches in a girl with a pineal cyst? Acta Paediatr 2013;102:e51-2.

19. Michielsen G, Benoit Y, Baert E, Meire F, Caemaert J. Symptomatic pineal cysts: Clinical manifestations and management. Acta Neurochir (Wien) 2002;144:233-42; discussion 242.

20. Peres MF, Zukerman E, Porto PP, Brandt RA. Headaches and pineal cyst: A (more than) coincidental relationship? Headache 2004;44:929-30.

21. Seifert CL, Woeller A, Valet M, Zimmer C, Berthele A, Tolle T, et al. Headaches and pineal cyst: A case-control study. Headache 2008;48:448-52.

22. Stevens QE, Colen CB, Ham SD, Kattner KA, Sood S. Delayed lateral rectus palsy following resection of a pineal cyst in sitting position: Direct or indirect compressive phenomenon? J Child Neurol 2007;22:1411-4.

23. Storey M, Lillimpakis K, Grandal NS, Rajaraman C, Achawal S, Hussain M. Pineal cyst surveillance in adults—a review of 10 years’ experience. Br J Neurosurg 2019;1-4.

24. Wisoff JH, Epstein F. Surgical management of symptomatic pineal cysts. J Neurosurg 1992;77:896-900.

How to cite this article: Milton CK, Pelargos PE, Dunn IF. Headache outcomes after surgery for pineal cyst without hydrocephalus: A systematic review. Surg Neurol Int 2020;11:384.