



Review Article

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

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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 the 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

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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 rates 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.^[12] 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].^[5,7,8,10,11,14,16-19,22]

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

Table 1: Included references.

Author date	Journal	Study type	Total reported subjects	Subjects meeting inclusion criteria
Klein and Rubinstein, 1989	J Neurol Neurosurg Psychiatry	Retrospective series	7	1
Fleege <i>et al.</i> , 1994	AJNR Am J Neuroradiol	Retrospective series	19	5
Michielsen <i>et al.</i> , 2002	Acta Neurochir (Wien)	Retrospective series	7	1
Mandera <i>et al.</i> , 2003	Childs Nerv Syst	Retrospective series	24	1
Stevens <i>et al.</i> , 2007	Child Neurol	Case report	1	1
Kahilogullari <i>et al.</i> , 2013	Childs Nerv Syst	Case report	1	1
Meyer <i>et al.</i> , 2013	Acta Paediatr	Case report	1	1
Majovsky <i>et al.</i> , 2017	World Neurosurg	Prospective	110	3
Majovsky <i>et al.</i> , 2017	J Clin Neurosci	Prospective	7	1
El Damaty <i>et al.</i> , 2019	World Neurosurg	Retrospective series	43	5
Koziarski <i>et al.</i> , 2019	Br J Neurosurg	Retrospective series	28	4
		Total	248	24

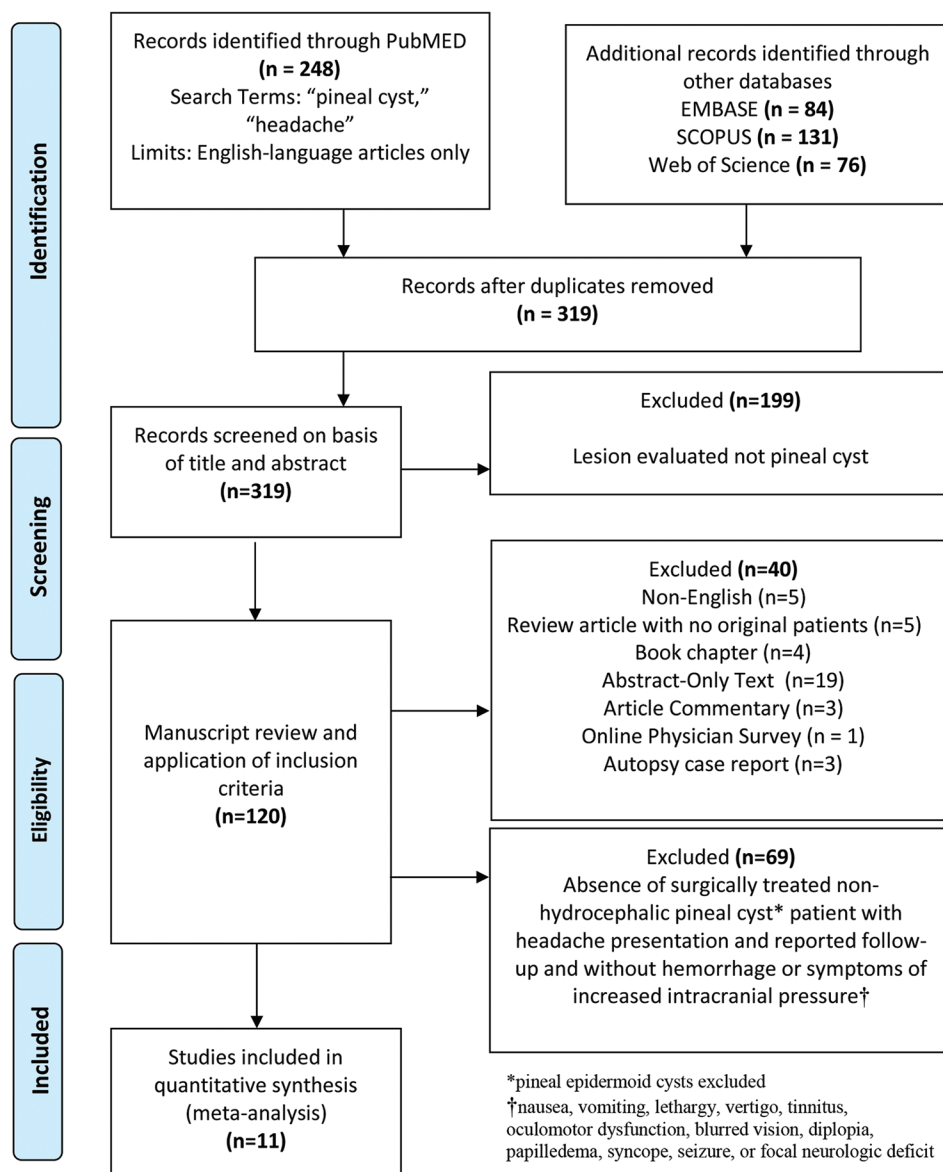


Figure 1: Prisma flow diagram depicting systematic review strategy.

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.^[7,14]

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^[5,14] or visual analog scale.^[16] 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				
	Author date	Journal	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?
Klein and Rubinstein, 1989	J Neurol Neurosurg Psychiatry	F	22	N		12	Headache	NR	Immediate post-operative follow-up; Lost to long-term follow-up	None	"After operation the headache cleared"	Yes
Fleege et al., 1994	AJNR Am J Neuroradiol	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
		F	35	1.2	NR		Headache	Supracerebellar infratentorial	3-5 months	small venous cerebellar infarction	"Presenting symptoms completely resolved"	Yes
Michielsen et al., 2002	Acta Neurochir (Wien)	F	27	2.0	48		Headache	Supracerebellar infratentorial	12 months	None	"Patient maintained their headache"	No
Mandera et al., 2003	Childs Nerv Syst	F	15	<2.0	NR		progressive headache	Supracerebellar infratentorial	31 months*	None	"Free of symptoms"	Yes
Stevens et al., 2007	Child Neurol	F	13	1.8	14		Headache	Supracerebellar infratentorial	1 month	None	"Headache free"	Yes
Kahilogullari et al., 2013	Childs Nerv Syst	F	13	1.6	36		progressive headache	Occipital transtentorial	6 months	None	"headache free"	Yes
Meyer et al., 2013	Acta Paediatr	F	14	NR	7		chronic intermittent headache	NR	NR	None	"After surgery headache symptoms resolved"	Yes
Majovsky et al., 2017	World Neurosurg	F	50	1.3	48		Worsening tension headache	Supracerebellar infratentorial	NR	None	"Headache improved"	Yes

(Contd...)

Table 2: (Continued).

Publication	Patient demographics				Clinical characteristics				Postoperative outcomes			
	Author date	Journal	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?
			F	23	2.3	36	Worsening tension headache	Supracerebellar infratentorial	NR	Hematoma	"Headache improved"	Yes
			F	23	1.4	12	Worsening tension headache	Supracerebellar infratentorial	NR	None	"Headache resolved"	Yes
Majovsky et al., 2017	J Clin Neurosci		F	22	1.4	NR	"Intractable headache"	Supracerebellar infratentorial	6-10 days	None	"Substantial improvement in presenting symptoms"	Yes
El Damaty et al., 2019	World Neurosurg		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
Kozlarski et al., 2019	Br J Neurosurg		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.^[24] 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.^[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.^[21]

Popular explanations for a causal link between pineal cysts and headaches in non-hydrocephalic patients include altered melatonin secretion and intermittent aqueduct obstruction.^[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.^[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.^[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.^[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.^[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.^[15]

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.^[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.

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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.